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TO STUDY THE EFFECTIVENESS OF ORAL AZITHROMYCIN IN THE TREATMENT OF UNCOMPLICATED ENTERIC FEVER AS COMPARED TO PARENTERAL CEFTRIAXONE

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CERTIFICATE

Certified that this dissertation titled **"TO STUDY THE EFFECTIVENESS OF ORAL AZITHROMYCIN AS COMPARED TO PARENTERAL CEFTRIAXONE IN THE TREATMENT OF UNCOMPLICATED ENTERIC FEVER",** is a bonafide work done by **Dr.POORNIMA. N,** Post graduate, ESIC Medical College & ESI PGIMSR, K.K. Nagar, Chennai, during the academic year 2011-2015.

Dr. Sowmya Sampath MD, DNB
Professor & Head,
Department of Paediatrics
ESIC Medical College &PGIMSR
K.K. Nagar,
Chennai

Dr. Shobhana. S MD, DCH
Associate Professor
Department of Paediatrics
ESIC Medical College & PGIMSR
K.K. Nagar
Chennai

Prof. Dr. Srikumari Damodaram, MS., MCh.
The Dean,
ESIC Medical College & PGIMSR
K. K. Nagar, Chennai

DECLARATION

I solemnly declare that this dissertation entitled **"To study the effectiveness of oral Azithromycin in uncomplicated Enteric Fever as compared to parenteral Ceftriaxone"** has been conducted by me at ESIC Medical College & PGIMSR, Chennai, under the guidance and supervision of **Dr.S.Shobhana, M.D., D.C.H.,** Associate Professor Department of Paediatrics, ESIC Medical College & PGIMSR, Chennai. This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.D. Branch VII (Paediatrics)**.

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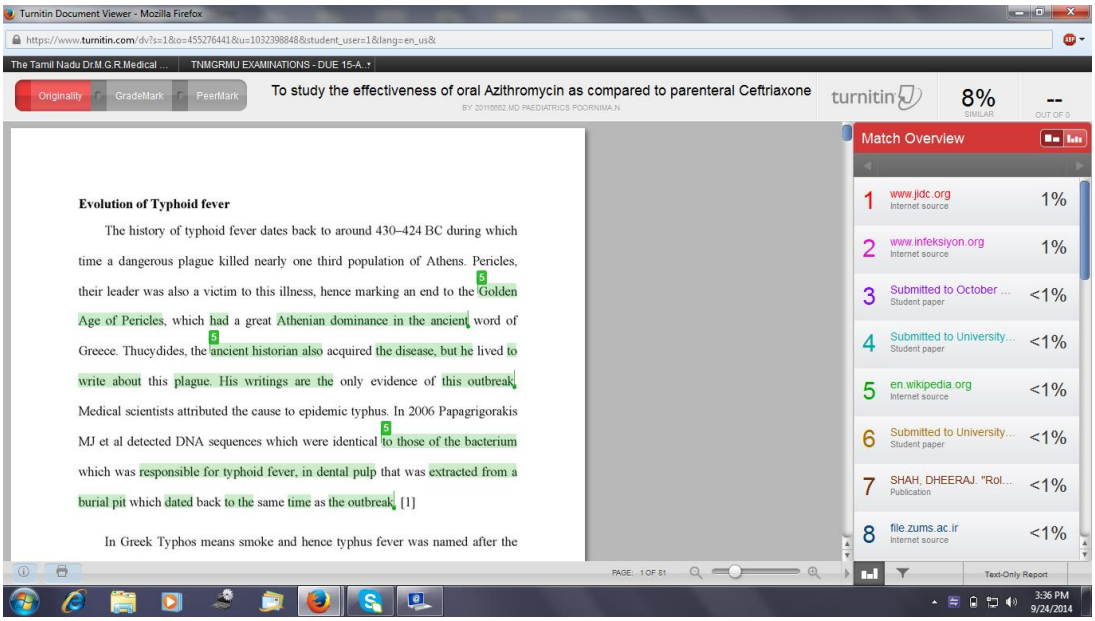
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Evolution of Typhoid fever
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CONTENTS

ABSTRACT

Objective: To compare the effectiveness of oral Azithromycin and intravenous Ceftriaxone in the treatment of uncomplicated enteric fever in children.

Methods: One hundred and twenty six children with proved enteric fever were enrolled in this study. They were randomized into two treatment groups. One group received oral Azithromycin (20mg/kg/day) and the other group received parenteral Ceftriaxone (75mg/kg/day), both of which were given for a duration of 7 days. The study population was observed for fever defervescence, duration of hospital stay and relapse. (In our study, 60 out of the 63 children in the Azithromycin group had defervesced within 7days of treatment whereas the remaining 3 crossed over. None in the Azithromycin group had relapsed. In the Ceftriaxone group, 59 out of the 63 children defervesced within 7days of treatment whereas remaining 4 cases were termed as treatment failures and required longer duration of the same drug.

Results: The mean time for defervescence was 3.68±2.109 and 4.08±1.903days in the Azithromycin group and Ceftriaxone group respectively. The mean duration of hospital stay was 7.35±2.604day in the Azithromycin group and 9.44±0.249days in the Ceftriaxone group. Among the 4 treatment failures in Ceftriaxone group, 2 cases relapsed within 4week follow up period. There was no relapse in the Azithromycin group.

Conclusion: Oral Azithromycin is as effective as intravenous Ceftriaxone in treating uncomplicated typhoid fever in children with respect to fever defervescence, duration of hospital stay and relapse.

INTRODUCTION

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Evolution of Typhoid fever

The history of typhoid fever dates back to around 430–424 BC during which time a dangerous plague killed nearly one third population of Athens. Pericles, their leader was also a victim to this illness, hence marking an end to the Golden Age of Pericles, which had a great Athenian dominance in the ancient word of Greece. Thucydides, the ancient historian also acquired the disease, but he lived to write about this plague. His writings are the only evidence of this outbreak. Medical scientists attributed the cause to epidemic typhus. In 2006 Papagrigorakis MJ et al detected DNA sequences which were identical to those of the bacterium which was responsible for typhoid fever, in dental pulp that was extracted from a burial pit which dated back to the same time as the outbreak.[1]

In Greek Typhos means smoke and hence typhus fever was named after the smoke that was thought to have caused it. Typhoid means like typhus. Hence this name was given to this disease. The first to differentiate clearly between typhus fever and typhoid in the year 1837 was William Wood Gerhard.

In 1856 William Bud, a British practitioner, demonstrated an agent in the stools of patients with typhoid, that carried the disease to other

patients. To prevent spread of the infection he had proposed boiling contaminated linen, chemically disinfecting the discharges from typhoid patients, having attendants wash their hands and also boiling of water and milk during an epidemic.

In 1879, Karl Joseph Eberth, doctor and student of Rudolf Virchow, discovered the bacillus in the abdominal lymph nodes and the spleen of patients with typhoid fever. His discovery was then verified and confirmed by German and English bacteriologists, including Robert Koch. The genus “Salmonella” got its name after Daniel Elmer Salmon who was an American pathologist. French physician Pierre Charles Alexandre Louis proposed the name “typhoid fever”.[2]

In 1906 George Soper of New York City's health department investigated six cases of typhoid that had occurred in one household. He learned that a recently employed Irish cook had left abruptly after a stay of 3 weeks. When he finally traced the cook he discovered that she had been the cause of seven epidemics of typhoid in 6 years. Her name was Mary Mallon, but she came to be known as Typhoid Mary. In all, she was responsible for spreading the infection to at least 122 people, including 5 deaths. Mary Mallon, the first known case of a healthy carrier in the United States, was kept in hospital for 3 years but she discharged herself and against medical advice, took a job involving the handling of food; this led to a further series of epidemics. Cholecystectomy was the only

known treatment for carriers at the time, but she did not get it done. She spent the last 23 years of her life in hospital.[2]

In 1937, Friz Kauffmann and Philip B. White in 1926 introduced the Kauffmann – White classification system after studying the antigenic structures of both typhoid and typhoid –like bacteria in detail. The isolation of Salmonella is based on this classification system which utilizes antigenic specificities of H, O and Vi antigens.[2]

Magnitude of the problem

Typhoid fever is a major global public health problem. In view of the similarities in clinical picture as seen with many other febrile infections, it is difficult to estimate its actual impact. The global incidence of typhoid fever was arrived at based on literature and large vaccine field trials. It has been estimated that 21.6 million cases and about 2.5 lakh deaths occur worldwide annually. Almost 80% of which occur in Asia and in developing countries such as India, its incidence varies from 102-2219/1 lakh population. In endemic areas, about 1/3rd to 1/4th of pediatric enteric fever cases are less than 5yrs with 6-21% cases being less than 2yrs of age.

The ratio of infection caused by S. typhi: S. paratyphi was about 10:1 in reports from most countries. The age group at risk of developing the infection during large outbreaks and in areas of endemicity and was 3

to 19 years. Nevertheless, clinically apparent bacteremia in children aged less than three years has been described from India, Bangladesh, Nigeria, Jordan, etc. Chronic carrier state has been observed in about 1-5% of patients who had suffered from acute typhoid infection. These individuals harbored the organism in the gall bladder. The risk of becoming a carrier was more in gall bladder disease, increasing with age and was greater in females when compared to men. [3, 4, 5, 6]

The Organism:

The organism implicated in the causation of enteric fever is Salmonella typhi, a gram negative bacillus. They vary in size between 1-3 micro meters to 0.5micro meters. They are motile with peritrichate flagella. They also possess fimbriae. They are aerobes and facultative anaerobes. The disease caused by Salmonella paratyphi A and B is similar to S. typhi but less severe.

Colony characteristics:

The colonies of Salmonella are classically described as smooth, non- hemolytic and non-lactose fermenting on various special culture media. [7]

Table 1: Clinical features of Typhoid fever in children.[8]

Symptoms	Signs
1. High grade fever	Toxicity
2. Anorexia	Coated tongue
3. Vomiting	Pallor
4. Diarrhoea	Rose spots
5. Abdominal pain	Abdominal distension
6. Constipation	Hepatomegaly
7. Headache	Splenomegaly

Complications of enteric fever in children:

The most common complications encountered in typhoid fever are (in order of decreasing presentation):

1. Central nervous system involvement is seen as psychosis, delirium, meningism, seizures; CNS infections like meningitis, subdural empyema, cerebral abscess, meningitis, ventriculitis. Other complications also seen are motor neuron disorders, ataxia and Guillain Barré syndrome.
2. Gastro intestinal system: Next most commonly involved is the GI system. The child can usually present with hepatitis, cholecystitis and paralytic ileus. Rarely seen are hepatic abscesses, splenic abscess, peritonitis etc.
3. Pulmonary involvement is seen as bronchitis, pneumonia and empyema or broncho pleural fistula.
4. The cardiac complications of typhoid fever include endocarditis, pericarditis, myocarditis and congestive cardiac failure.
5. Genitourinary involvement is seen in less than 1% of the cases, and includes UTI, renal abscess, pelvic infections, testicular abscess, epididymitis and prostatitis.
6. Bone and joint involvement is seen as either septic arthritis or osteomyelitis.

7. Other less commonly encountered complications but described in literature are cutaneous vasculitis, psoas abscess, gluteal abscess and Hemophagocytosis syndrome. [8]

Emergence of resistance and Quest for newer drugs

In 1948, Theodore Woodword showed that Chloramphenicol sterilized the blood culture of enteric fever patients. In view of this property, this drug was most commonly prescribed for treating typhoid fever. Within 2yrs (1950) of its advent, S. typhi isolates resistant to Chloramphenicol started appearing in UK, this was attributed to its indiscriminate usage. In the 60s, sporadic cases of Chloramphenicol resistant typhoid fever were reported from all over the world, including India. The first epidemic of chloramphenicol resistant enteric fever occurred in Mexico in 1972, followed by India (1972), Vietnam (1973) and Korea (1977). [3, 4]

Cotrimoxazole was used as an effective alternative to Chloramphenicol in treating these resistant strains till 1975. But resistance to Cotrimoxazole started appearing in France. Strains resistant to all 3 first line drugs i.e. Ampicillin, Cotrimoxazole and Chloramphenicol, started appearing by late 1980s. MDRST (multidrug resistant salmonella typhi) was seen in epidemic proportions for which fluoroquinolones were used worldwide. The first case of S.typhi resistant to fluoroquinolones was reported in 1992 from the UK and

fluoroquinolone resistant cases were also increasingly reported from several other countries and India. [3, 4]

With the increasing development of Nalidixic acid (Quinolone) resistance among S. typhi, 3rd generation Cephalosporins are being used in the management of MDRST.

Intravenous Ceftriaxone administration is associated with high cost, prolonged hospitalization and morbidity due to intra venous drug use. Of late Salmonella strains resistant to Ceftriaxone have started appearing.[3, 4, 5]

In view of emergence of MDRST and NARST (Nalidixic acid resistant salmonella typhi), a number of studies were carried out worldwide to study the clinical and epidemiological profile of MDRST and NARST, including the drug sensitivity and resistance patterns of S. typhi, thereby beginning the quest for newer drugs.

The Indian Scenario

In India, MDR Salmonella typhi (MDRST) was first reported in 1988 from Mumbai. Again in March 1990, an outbreak of MDRST occurred in Mumbai which was called Dombivli fever. In the same year there was an outbreak of MDRST in New Delhi. The S. typhi strains in these two outbreaks were found to be sensitive to ciprofloxacin. MDRST was also reported in the mid-1990s from Bangalore which was found to

be as high as 95%. In 1999, similar resistance to the 3 first line drugs was reported from Manipal. It was found that all these strains were sensitive to Fluoroquinolones and Ceftriaxone. During these outbreaks, Ciprofloxacin was considered as the first drug of choice for its high cure rate without any relapse or carrier state. Over the subsequent few years, there was an increase in Ciprofloxacin resistance.

In 2000, Das et al from Orissa found that 2.5% of S. typhi strains were resistant to Ciprofloxacin. In a prospective study done by Kumar et al in Delhi, there was a sequential increase in MDRST from 34% to 66% over 10 years (1999-2009). They also reported a gradual increase in Fluoroquinolone resistance over these 7 years.

As the years progressed, several isolated reports of resistance to Ceftriaxone were reported from different parts of India. These observations of increasing ciprofloxacin resistance and early evidence of Ceftriaxone resistance correspond with the global picture. [4, 5, 6]

Drugs used in the management of typhoid fever:

Chloramphenicol:

Mechanism of action of Chloramphenicol is by inhibition of microbial protein synthesis. Chloramphenicol inhibits peptidyl transferase step of protein synthesis by binding reversibly to 50S subunit of the bacterial ribosome. It is bacteriostatic and has broad-spectrum activity

against both aerobic and anaerobic organisms; and gram-positive and gram-negative organisms. Minimum inhibitory concentration for most gram positive organisms is 1–10 μg/mL, and for gram-negative bacteria it is 0.2–5 μg/mL. Resistance to Chloramphenicol occurs due to the production of acetyl transferase by the organism which is a plasmid-encoded enzyme resulting in drug inactivation. Its therapeutic dose is 50–100 mg/kg/d. One gram of the drug achieves a serum concentration of 10-15μg/mL. Its prodrug is Chloramphenicol palmitate which gets hydrolyzed in the intestine to Chloramphenicol. Chloramphenicol succinate is also a prodrug used in parenteral preparations, which is hydrolyzed to Chloramphenicol, producing serum concentrations lower than that achieved with oral drug. It has a large volume of distribution. Penetration of the drug through the cell membranes occurs readily. Inactivation of the drug occurs in the liver both by glucuronic acid conjugation and by conversion to inactive aryl amines. Drug elimination occurs in the urine, bile and feces. Drug dose needs to be adjusted in hepatic failure, newborns and preterm infants. Chloramphenicol is rarely used now a days because of the rapidly developing resistance and toxicities.[9]

Cotrimoxazole:

Trimethoprim is a tri methoxy benzyl pyrimidine and its mechanism of action is by selective inhibition of bacterial dihydrofolic acid reductase, an important step in the synthesis of nuclear material. Pyrimethamine is also a benzyl pyrimidine. It acts by selectively inhibiting the dihydrofolic acid reductase of only microorganisms. The combination of a Sulfonamide with Trimethoprim or Pyrimethamine results in synergism thereby enhancing drug potency. The combination becomes bactericidal though the individual drugs if used alone are bacteriostatic. It is usually given orally though injectable formulations of Trimethoprim-sulfamethoxazole are currently available. Both the drugs are excreted through urine and require dose adjustments in cases with decreased creatinine clearance. Drug resistance to Cotrimoxazole can be due to:

1. Dihydrofolate reductase over production OR
2. Decreased drug binding due to production of an altered reductase OR
3. Decreased cell permeability OR
4. By plasmid-encoded Trimethoprim-resistant dihydrofolate reductases.

Trimethoprim causes leukopenia, granulocytopenia and megaloblastic anemia due to its antifolate activity.[10]

Fluoroquinolones:

Fluoroquinolones are synthetic fluorinated analogs of Nalidixic acid. Its mechanism of action is mainly by inhibition of bacterial DNA synthesis which is brought about by blocking DNA gyrase and topoisomerase IV. This prevents the positively supercoiled structure of DNA from relaxing, which has a role in normal transcription and replication of the nuclear material. All these interfere with the normal replication and distribution of nuclear material during cell division.

Resistance is either due to one or more point mutations in quinolone binding region of the target enzyme or a change in permeability of the organism. Recently two types of plasmid mediated resistance have been described. One type utilizes Qnr proteins, which protects the DNA gyrase from fluoroquinolones. The other type is a variant of aminoglycoside acetyl transferase capable of making modifications to Ciprofloxacin. Cross resistance is a well-known entity in this group of drugs.

Their bioavailability is about 80–95% after oral administration and has a large volume of distribution. Its t½ is between 3-10 hours. These drugs have relatively long plasma t½ enabling once a day dosing.

Dose needs to be adjusted in renal failure since the main route of excretion is through urine.[10]

Ampicillin:

Its antibacterial spectrum comprises those of penicillin as well as has gram-negative coverage. They are susceptible to hydrolysis by beta lactamases. Hence it is usually administered in combination with a beta lactamase inhibitor like Clavulanic acid, Tazobactam or Sulbactam to extend its spectrum of activity. Non allergic rash is caused by Ampicillin and amoxicillin. Inappropriate prescription of amino penicillins for viral illness results in such a rash frequently.[11]

Table 3: Treatment of uncomplicated typhoid fever: [8, 12]

Susceptibility	**Optimal therapy**			**Alternative effective drug**		
	Antibiotic	**Daily dose (mg/kg)**	**Days**	**Antibiotic**	**Daily dose (mg/kg)**	**Days**
Fully sensitive	Chloramphenicol (or) Amoxicillin	50-75 75-100	14-21 14	Fluoroquinolones, e.g., Ofloxacin (or) Ciprofloxacin	15	5-7
Multidrug resistant	Fluoroquinolones (or) Cefixime	15 15-20	5-7 7-14	Azithromycin (or) Cefixime	20 15-20	7 7-14
Quinolone resistant	Azithromycin (or) Ceftriaxone	8-10 75	7 10-14	Cefixime	20	7-14

Ceftriaxone Vs Azithromycin

Ceftriaxone

It is a 3rd generation Cephalosporin with broad-spectrum of activity against both gram positive and negative organisms. Its main mechanism of action is by inhibiting the bacterial cell wall synthesis by binding to penicillin binding proteins. It is bactericidal but is inactive against organisms producing extended spectrum beta lactamases.[11]

Azithromycin

Azithromycin is a macrolide antibiotic with the advantages of excellent intracellular penetration and long t½ of about 72hrs.This helps in administering the drug once a day. Several clinical trials have studied and found that it is more potent than first-line drugs and other macrolides in treating salmonella infection. It has a MIC of 8μg/mL (range 4 to 16μg/mL).

Food, aluminium and magnesium antacids interfere with its absorption from the gut.[9]

Prevention of typhoid fever

The major route of transmission of typhoid fever is feco-oral. Infection can be acquired by consuming water or food that is contaminated by the organism. Therefore main modalities of prevention

are by promoting personal hygiene, ensuring access to safe and clean drinking water and also by propagating clean food handling practices.

- Safe water: Typhoid fever can be acquired by drinking unclean water. Every effort must be taken towards providing clean, chlorinated water to the community. The water should be clear and non-foul smelling. In the community, people should take care of the hygiene around water sources and drinking water should be boiled before consuming.

- Food safety: At home, the person involved with cooking should ensure proper hand washing before cooking and raw fruits and vegetables should be washed well and cooked well before consumption. As mentioned earlier, Typhoid Mary was responsible for epidemics as a chronic carrier, by way of serving contaminated food. Hence people involved in food industry should be screened for chronic carrier state and should not be allowed to resume their duties until they have had three negative stool cultures taken at least one month apart.

- Sanitation: Proper sanitation plays an important role in breaking the chain of transmission of the infecting pathogen. This can be achieved by:

    * Sanitary latrines should be used for defecation.

* Ensure safe human waste disposal.

* Discourage the use of human excreta as fertilizers

- Health Education: has a pivotal role in preventing any communicable disease. Health education should address all age groups and all socio economic strata. It should aim at promoting personal and community hygiene, use of clean water, use of sanitary latrine, proper hand washing techniques, etc. People should be educated regarding the use of freshly prepared food rather than reheating them. Health education can be imparted to the community by way of role plays, community talks, mass media like newspapers, TV, radio and internet; and school health programmes. [13]

REVIEW OF LITERATURE

REVIEW OF LITERATURE

1. Articles related to clinical features of typhoid fever in children

In a study conducted by Ramaswamy et al[14] from south India, which spanned over 3years (2005-2008), it was found that three hundred and sixteen children were treated as enteric fever out of forty five thousand one hundred and ninety six hospital admissions, this accounted for seven per one thousand admissions. Among the 316 children enrolled, male: female ratio was 1.29:1. Maximum number of cases (38%) were found to occur between January to April. Most common age group affected was 5-10yrs (33.5%) with 1.8 % cases being less than 1 year of age, 16 % cases between 1-2 years, 32 % cases between 2-5 years and 15.8 % cases more than 10 years of age. The predominant symptom and sign was vomiting and hepatomegaly seen in 49% and 71% cases respectively. Other symptoms and signs observed were diarrhea, splenomegaly, and toxemia; observed in 29%, 34% and 16% cases respectively. Leukocytosis was more common than leucopenia, seen in 12% and 8% of the cases respectively. They had found statistically significant eosinopenia in 72 % of cases. On analyzing the liver enzyme levels they found mild elevation of serum transaminases in majority of the cases (60%). On reviewing the ultrasound abdomen report they found thirteen children to have free fluid in the abdomen and about fifteen children to have gall bladder disease, which was evidenced by gall bladder hydrops, thickening and sludge. The complications encountered

in their study group was Systemic inflammatory response syndrome, hepatitis, septic shock, meningitis, GI bleed, osteomyelitis, myocarditis and Infection associated hemophagocytic lympho histiocytosis.

Lalitha et al[15], in their retrospective study had reviewed case records of children in the age group one month to 18 years with culture proven typhoid fever, between January to December 2007. They observed that during the specified period, 100 children had culture proven Salmonella infection out of thirteen thousand two hundred and sixty five admissions, male: female ratio being 2:1. Majority (51%) of the children was below 5 years, 32% were between 5 and 10 years and 17% were above 10 years. Cases clustered between the months of September and December. Fever (100%), vomiting (54%) and loose stools (31%) were the predominant symptoms seen. Common clinical signs observed were hepatomegaly (72%), splenomegaly (31%), and coated tongue (24%). Eosinopenia was observed in 67%. None had sonographical evidence of cholelithiasis.

In a retrospective study by Gosai et al [16] done at Ahmedabad, case records of 150 children with clinical enteric fever or proven cases of typhoid fever, were reviewed over a period of one year. They observed that there were 88 male and 62 female patients, in the age group 2-12 years. Fever, abdominal pain, vomiting and headache were the predominant symptoms observed. Hepatomegaly was more common than

splenomegaly. Relative bradycardia and rose spots were rarely seen in children. Fever, Toxic look, coated tongue and hepatosplenomegaly were common clinical signs of clinical presentation in children. Hepatitis, Bronchitis and Encephalopathy were commonly observed complications of Multidrug resistant typhoid fever in this study.

A retrospective analysis of 106 individuals who were culture positive for Salmonella typhi was done by Kumar et al[17] at Manipal. They observed that majority (78.3%) was males and 21.7% were females. Most common age affected was between 15-30 years. The mean age of the patients was 28.8±1.32 years. The average duration of hospital stay was 8.7 days. All patients in the study had fever. The common symptoms were headache, vomiting, abdominal pain and diarrhea which were seen in 63 (59.4%), 30 (28.3%), 21 (19.8%) and 29 (27.4%) patients, respectively. They observed splenomegaly in 47 (44.3%), hepatomegaly in 42 (39.6%) while hepatosplenomegaly was seen in 23 (21.7%). Abdominal tenderness was another common presenting sign seen in 23 (21.7%) of cases. Widal was concomitantly positive in 73 (68.9%) cases. Liver enzymes (alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase) were raised in 52 (49.1%) patients. Complications were very few. Only one patient each had myocarditis, encephalitis, gastrointestinal bleed and gastrointestinal perforation as complications.

2. Articles related to Epidemiology

Ram et al[18] conducted a study in a small slum of Bangladesh to find out risk factors for typhoid fever in that part of the world. They found that drinking unboiled water at home; foul-smelling water source, eating substandard ice creams, milk products, milk sweets, consuming fruits and vegetables without washing were all associated with the illness. Using a latrine for defecation was found to be significantly protective.

Following typhoid fever outbreak in a slum in West Bengal, in February 2007, Bhunia et al[19] attempted to find out the cause for the outbreak. They identified that the suspected cases clustered around three public taps and were consuming milk products from a common sweet shop. The food handler in that particular sweet shop had suffered from enteric fever in January that year and was probably the Typhoid Mary in these cases. The pipelines of drinking water and sewage system ran next to each other and the water from these pipes had revealed fecal contamination.

3. Articles related to Azithromycin use in typhoid fever

Anju et al[20] conducted a multicenter study to evaluate the efficacy and safety of Azithromycin in the management of uncomplicated typhoid fever. Mean day of response was 3.45±1.97 days. They observed 100% clinical and microbiological cure without any relapse. None in this study had any adverse events. Hence they concluded that oral Azithromycin was safe and effective in the treatment of uncomplicated typhoid fever.

Dheeraj Shah[21] included 7 randomized trials in his systematic review. The seven trials had enrolled seven hundred and seventy three confirmed cases of uncomplicated typhoid or paratyphoid fever. Three trials each were conducted in Vietnam, Egypt and one reported from India was a multicentric trial. Three out of the seven trials included adults only, two trials included children only, and two other trials included both. Many cases included in these trials had infections with MDRST and NARST. Ceftriaxone and Ofloxacin were compared with Azithromycin, in 2 trials. Azithromycin was compared with Ciprofloxacin in one trial, with Gatifloxacin in a second trial and with Chloramphenicol in the third one.

On comparing with Fluoroquinolones, Azithromycin significantly reduced clinical failure, duration of hospital stay and number of relapse. The authors concluded that Azithromycin was more effective than fluoroquinolones for treatment of enteric fever including MDRST and

NARST and may be much better than Ceftriaxone in reducing the number of relapse.[21]

In a study done by Hussain et al[22] in Shaikh Zayed Hospital, Lahore, Pakistan, during the year 2011, 83 confirmed cases of typhoid fever were enrolled and treated with oral Azithromycin 20mg/kg/day for 7days.Out of the 83 children enrolled, 75(90.36%) completed the study. Male to female ratio was 1.6:1 in the age group of 8-12 years. S.typhi was isolated in 5(6.67%) cases and all achieved bacteriological cure by seven days. Mean duration of fever at presentation was 5±3.07 days. Seventy one cases had clinical cure with mean day of response being 4 days. The authors concluded that Azithromycin was found to be safe and effective in the treatment of uncomplicated typhoid fever in a dose of 20mg/kg/day per oral once a day for seven days.

4. Articles comparing Azithromycin with Fluoroquinolones

Girgis et al[23], in their study conducted at Egypt in 1999, comparing Azithromycin and Ciprofloxacin in uncomplicated typhoid fever in adults observed that the time taken for defervescence in Azithromycin group was 3.8 ± 1.1days and 3.3 ± 1.0days with Ciprofloxacin. There were no relapses in either group. They concluded that Azithromycin and Ciprofloxacin had similar efficacy, against both sensitive organisms and MDRST.

In yet another study by Parry et al[24] from Vietnam, Azithromycin was studied as a single drug as well as in combination with Ofloxacin and with Ofloxacin alone, in three groups of children respectively. It was found that the clinical cure rate was 64%, 76% and 82% with Ofloxacin, Ofloxacin-Azithromycin combination, and Azithromycin alone, respectively (P 0.053). The mean fever clearance time for patients treated with Azithromycin [5.8±0.7days] was shorter than that for patients treated with Ofloxacin-Azithromycin [7.1±1.1days] and Ofloxacin [8.2±1days] ($P < 0.001$). Following this study Parry et al found that uncomplicated typhoid fever can be treated with successfully a 7-day course of Azithromycin.

In a prospective, randomized, open labelled study conducted by Chandey et al[25], to compare the efficacy and safety of Azithromycin with Ofloxacin in patients with uncomplicated typhoid fever, 40 adult patients

with bacteriological or serological diagnosis of typhoid fever were included from Medicine out-patient department at Government medical college, Amritsar, India. The study population was randomized into two groups of twenty patients each. Group 1 was treated with Ofloxacin and group 2 with Azithromycin. Nineteen out of 20 patients from group one defervesced with mean fever defervescence of 3.68 days while all 20 patients from group two defervesced with a mean fever defervescence of 3.65 days. They concluded that both Ofloxacin and Azithromycin were almost equally efficacious and safe in treatment of typhoid fever with no major adverse effect and Azithromycin is an effective alternative in conditions where Ofloxacin is contraindicated as in quinolone resistant cases of typhoid fever, children and pregnant women.

5. Articles comparing Azithromycin with Chloramphenicol

Butler et al [26] randomized 77 adult patients with typhoid fever into two treatment groups, Azithromycin and Chloramphenicol. 42 patients in Azithromycin group received the drug at 500mg/day PO OD for 7days and 35 patients in the Chloramphenicol group received the drug at 2-3g PO OD in four divided doses for 14days. 37 patients (88%) in the Azithromycin group and 30 patients (86%) in the chloramphenicol group responded within 8days. By 14days after start of therapy, all patients in the Azithromycin group (100%) and all except 2 cases in the Chloramphenicol group (94%) were cured. They concluded that Azithromycin given once daily for 7days was effective in treating both Chloramphenicol resistant as well as Chloramphenicol sensitive Salmonella infection.

6. Articles comparing Azithromycin with Ceftriaxone

In 2004 Frenck et al[27] conducted a study to compare the effectiveness of oral Azithromycin and parenteral Ceftriaxone in the treatment of uncomplicated enteric fever. They had enrolled 149 children and adolescents between 3–17 years of age with clinical typhoid fever. These children were randomized into two treatment groups. One group received oral Azithromycin 20mg/kg/day OD and the other group received parenteral Ceftriaxone 75mg/kg/day. Both the drugs were given for duration of 5days. Complete cure was observed in 30 (94%) of 32 patients in the Azithromycin group and 35 (97%) of 36 patients in the Ceftriaxone group. Mean fever clearance time was 4.5±1.9 days in the Azithromycin group and 3.6±1.6 days in the Ceftriaxone group. Mean time to achieve microbiological cure was longer in the Azithromycin group than in the Ceftriaxone group. None in the Azithromycin group relapsed as against 6 relapses in the Ceftriaxone group. They concluded that a 5-day course of Azithromycin was an effective treatment for uncomplicated typhoid fever in children and adolescents.

STUDY JUSTIFICATION

STUDY JUSTIFICATION

Enteric fever is endemic in most parts of India. With the changing pattern in the presentation of enteric fever in different age groups and the sensitivity trends of S.typhi, pediatricians are faced with multiple challenges in their day to day practice.

Enteric fever still continues to be a major global public health problem despite the development of newer antibacterial drugs, the recent upsurge in multidrug resistant S.typhi infection has made the treatment of enteric fever a difficult problem.

With the rise in MDRST and NARST, parenteral Ceftriaxone is being increasingly used for the management of typhoid fever in children, which is associated with prolonged hospitalization, morbidity due to intravenous drug administration and loss of school days for children, loss of working days and hence loss of pay for parents.

Most parents of the children coming to our hospital are working mothers, who are already struggling to make the ends meet.

Before planning this study, the practice in our hospital was to treat all cases of Enteric fever with intra venous Ceftriaxone. We noticed several morbidities in children related to IV administration of the drug like pain, fever due to thrombophlebitis etc. We also observed that the families had to struggle to cope up with taking care of the hospitalized

sick child as well as to make arrangements to manage other family members at home. They had to keep themselves away from work thereby losing their income too. An effective orally available drug for enteric fever would be able to overcome at least some of the problems faced by the family.

Hence this study was undertaken to find out if oral Azithromycin is effective in reducing the time taken for defervescence and in reducing the duration of hospitalization.

MATERIAL AND METHODS

MATERIAL AND METHODS

Aims and Objectives

Aim of the study:

To study the effectiveness of oral Azithromycin as compared to parenteral Ceftriaxone in the treatment of uncomplicated Enteric fever.

Objectives of the study :

Primary objective: is to compare the effectiveness of oral Azithromycin and intravenous Ceftriaxone in the treatment of uncomplicated enteric fever in children.

Secondary objective: is to study the clinical and epidemiological profile of enteric fever in children.

Methodology

Study design:

Prospective, Randomized open labeled study

Place of study:

Department of Pediatrics, ESIC Medical College & PGIMSR, K.K Nagar, Chennai – 78

Period of study:

July 2013 – August 2014

Sample size:

63 in each group. The sample size was calculated by Convenient sampling method with OR – 6 and CI 95%, using openepi software.

Sample size calculation

2-sided significance level(1-alpha):	95
Power (1-beta, % chance of detecting):	80
Ratio of sample size, Unexposed to Exposed:	1
Percent of Unexposed with Outcome:	5
Percent of Exposed with Outcome:	24
Odds Ratio:	6
Risk/Prevalence Ratio:	4.8
Risk/Prevalence difference:	19

	Kelsey	**Fleiss**	**Fleiss with CC**
Sample Size - Exposed	54	53	63
Sample Size-unexposed	54	53	63
Total sample size	**108**	**106**	**126**

Study population:

The study population included all Paediatric ward in patients between 2 to 12 years of age with proven typhoid fever.

Inclusion Criteria:

Children admitted to the Pediatric ward with fever and

1. A positive Widal test or with rising titres of O and H antigens. OR

2. Blood / urine / stool culture positive for Salmonella

Were included in the study.

Exclusion Criteria:

1. Children with complications such as jaundice, severe gastrointestinal bleeding, myocarditis, intestinal perforation, renal failure, pneumonia, an altered level of consciousness or shock, etc.

2. Hypersensitivity to either of the drugs &

3. Lack of parental consent.

Were excluded from the study.

Procedure

Among the children presenting with fever, a detailed history taking and complete clinical examination was done. After obtaining consent from the parents, blood samples were drawn for complete blood counts, Widal test, blood culture and sensitivity, and also for other tests (smear for MP, Dengue serology etc.) to rule out other causes of acute febrile illness. Based on the duration of fever, urine and stool cultures were also done.

Once the investigation results were obtained, only proven cases of typhoid fever (i.e. positive Widal test or culture positive for Salmonella) were selected. **Informed consent was obtained from the parents before recruiting their children into this study**. All clinical findings, results of investigations, treatment details and follow up were documented in a pre-structured study proforma.

The children were divided into two groups by lots method. The lots were prepared as blocks of five in each treatment group. Closed envelopes containing the treatment group into which the child would fall comprised the lots. The children or their parents picked up the lot and the child was treated as per the treatment mentioned in the envelope.

Children under the Ceftriaxone group were administered Inj. Ceftriaxone 75mg/kg/day BD for seven days. And those under the Azithromycin group received Azithromycin suspension or tablet 20mg/kg/day as a single dose for seven days. Children in both the groups were subjected to clinical examination daily during their hospital stay and were observed for fever clearance. When there was failure to respond to either drug by seven days as evidenced by persistence of fever, it was considered as treatment failure.

Children who failed to respond to Azithromycin crossed over to Ceftriaxone and were treated with the above mentioned dose of Ceftriaxone till twenty four to forty eight hours after defervescence.

Children who failed to respond to Ceftriaxone were considered as treatment failure and continued to receive the same dose of Ceftriaxone till twenty four to forty eight hours after defervescence.

When defervescence occurred within seven days, children in the Azithromycin group were observed for 24hrs after fever clearance and discharged with the drug to be continued at home for the remainder days and were asked to review if fever recurred. But children in the Ceftriaxone group required hospital stay of seven days for completion of treatment, despite fever clearance.

After discharge the children in both the groups were reviewed at thirty days for a stool culture or earlier if they had recurrence of fever. Children who had recurrence of fever were again investigated for typhoid fever and if positive were considered as relapse.

Material used in this study:

Complete blood counts:

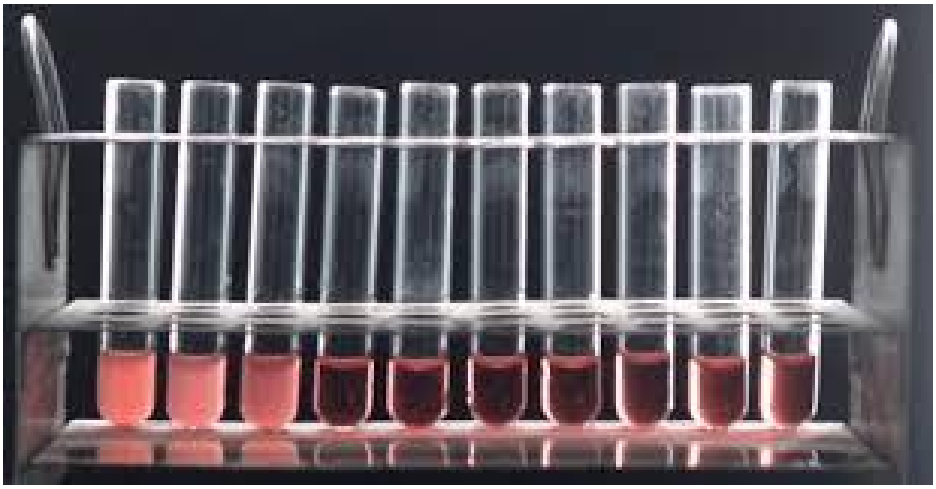
This was done using automated five part cell counter and the results were analyzed by flow cytometry.

Diagram 1: 5 Part cell counter used

Widal test:

It can be done in two ways – as tube agglutination and slide agglutination test. In our study, serological diagnosis of typhoid fever was made by using tube agglutination test. This test was named after Georges Fernand Isidore Widal, a French physician and bacteriologist. The principle behind this test is that patients with active Salmonella infection would express antibodies in their sera which react and agglutinate serial doubling dilutions of killed, colored Salmonella antigens. S.typhi O and S.typhi H antigens are prepared using Salmonella typhi 901 strain. The antigen O of S. typhi and that of paratyphi A and B have cross-reactivity with each other. The control tubes are examined first, which will not show any agglutination. The O antigen agglutination is seen as a “matt” or “carpet” at the bottom of the tube. The H antigen agglutination is seen as loose, wooly or cottony. The highest dilution of serum producing a positive agglutination is considered as titre. The titres for all the antigens are made note of.

Diagram 2: Widal test - tube agglutination test



Interpretation of Widal test: A Single titre is usually not of much importance. A rise in titre is more significant than a one test value. A titre is said to be significant if it is 100 or more for O antigen and 200 or more for H antigens.

There will be no rise in titre if the patient was already treated with antibiotic, instead there may be fall in titre. Results may not be positive even in patients treated with antibiotics in early stages of the illness.

False positive reactions are seen in vaccinated individuals, this can be differentiated from true typhoid illness by repeating this test after one week. A rising titre will be seen in true untreated infection whereas vaccinated individuals show no rise in titre.

Anamnestic reaction is seen in individuals with past salmonella infection. These individuals develop antibodies against Salmonella when they acquire infection with closely related organism. This reaction is identified by repeating the test after a week and demonstrating a lack of rise in titre. False positive reactions are observed if the antigen suspension contains fimbrial antigen.

Blood culture:

Under all aseptic precautions 2ml blood was drawn by venipuncture and was inoculated immediately onto a blood culture bottle (Diagram 2). The sample bottles were sent immediately to the microbiology laboratory, where these bottles were incubated at 37°C and checked for biochemical reactions like gas formation, turbidity and other evidence of growth after one, two and three days. When there was no evidence of growth even after 72 hours, the culture was reported as sterile

Diagram 2: Culture bottle used

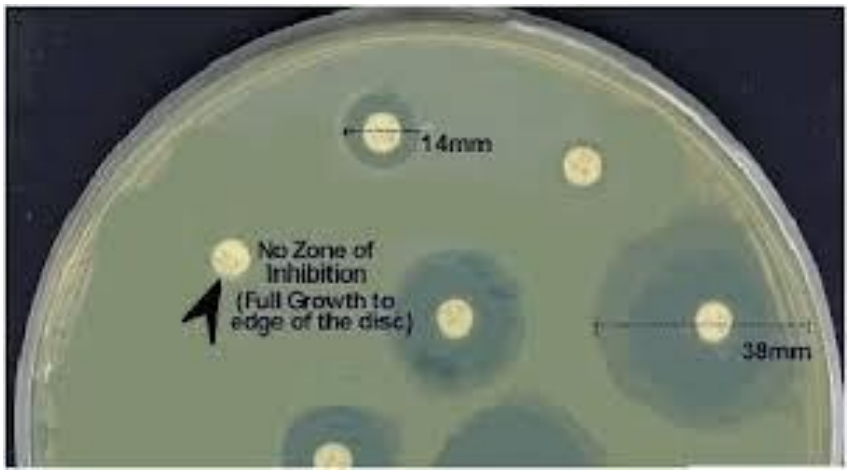
Diagram 4: Incubator used

Drug sensitivity:

After confirming the growth, antibiotic sensitivity was done using Kirby-Baur technique on Muller-Hinton agar. A loopful of growth was taken from the agar and inoculated in peptone water; after 10 minutes, this peptone water was poured over the Muller-Hinton agar to cover its entire surface; the excess peptone water was poured into the bottle.

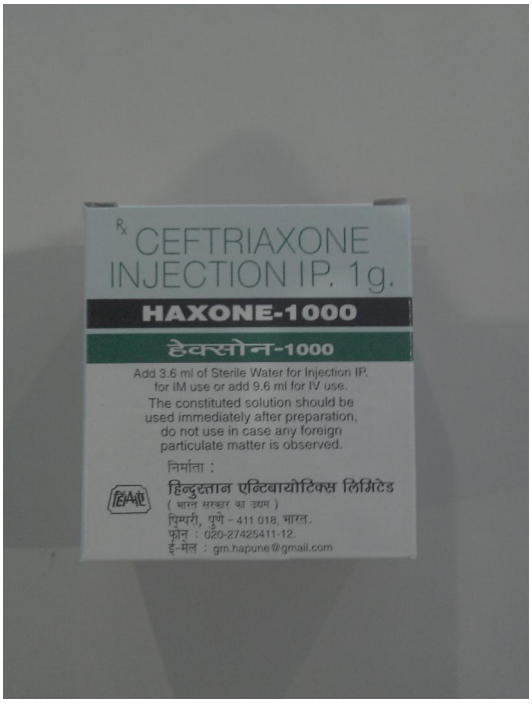
Then antibiotic discs like ampicillin, chloramphenicol, Nalidixic acid etc., were plated and incubated for 24 hours at 37□C. Then zone of inhibition was measured and results were interpreted.

Diagram 5: Drug sensitivity testing by disc diffusion



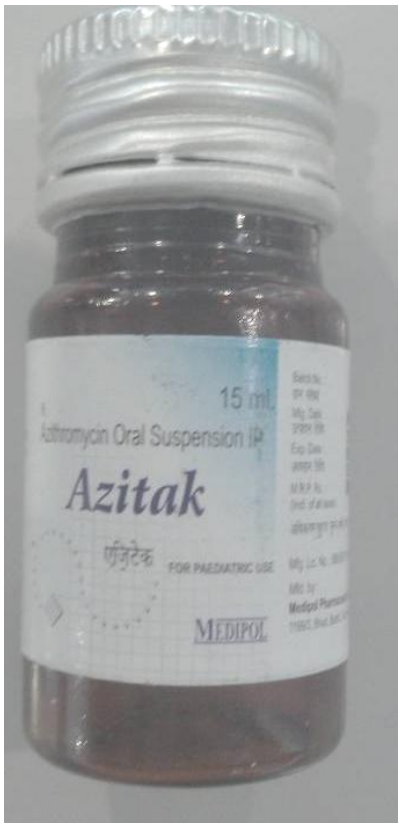
Ceftriaxone injection used:

Diagram 6: Ceftriaxone injection



Azithromycin tablets and suspension used:

Diagram 7: Azithromycin preparations used



Outcome measures:

The effectiveness of the treatment was assessed by the:

a) Time taken for fever clearance.

b) Duration of hospital stay and

c) Relapse

Statistical Analysis used:

In the above study, statistical methods were applied for quantitative data and qualitative data. Quantitative data was presented by N, Mean, Standard Deviation and Range. For qualitative data, frequency count N and percentage were tabulated in tables.

To analyze the data, appropriate statistical tests were applied. To compare the difference between two means, independent t test was used.

All the statistical analysis had been done by using statistical software SPSS (version 16.0). Other data was displayed by various tables and charts by using Microsoft excel (windows 7).

*Significant at $p < 0.05$

**very significant $p < 0.01$

***highly significant $p < 0.001$

RESULTS

RESULTS

On analysis of 126 cases enrolled in this study, the following observations were seen,

DEMOGRAPHIC FACTORS

Age Distribution:

Among the 126 participants enrolled in the study, the mean age was 6.98±3.25years. Out of which 44.4% were in the age group 2-6years and 55.6% in the age group 7-12years.

Mean age in Azithromycin and Ceftriaxone groups were 7.21±3.26years and 6.75±3.24years respectively. In the Azithromycin group, about 40% (n=25) cases were between 2-6years and 60% (n=38) were between 7-12years. In the Ceftriaxone group, about 49.2% (n=31) cases were between 2-6years and 50.8% (n=32) cases were between 7-12years.

Figure 1: Age distribution (n=126)

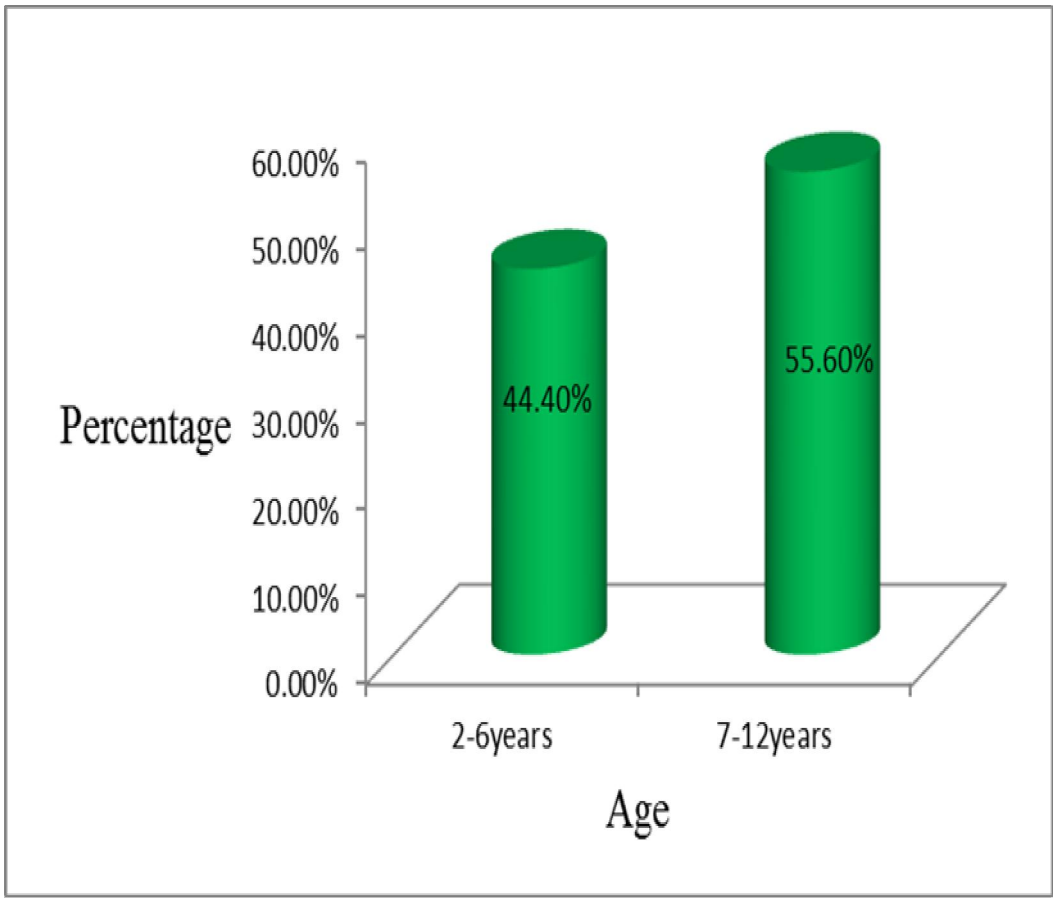
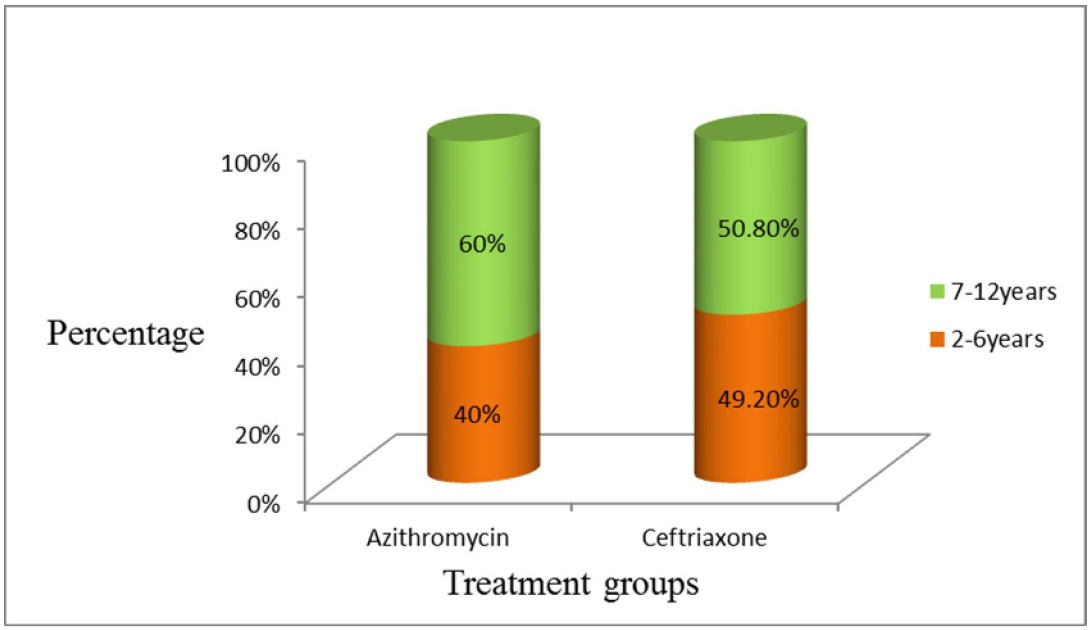


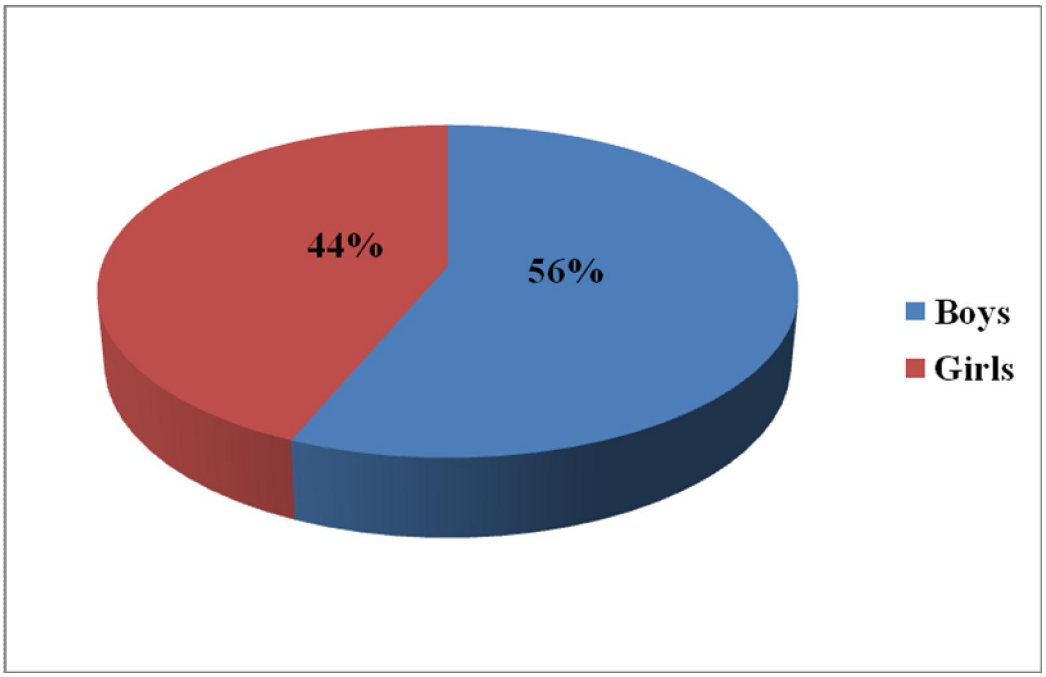
Figure 2: Age distribution (Azithromycin vs Ceftriaxone)



Gender Distribution:

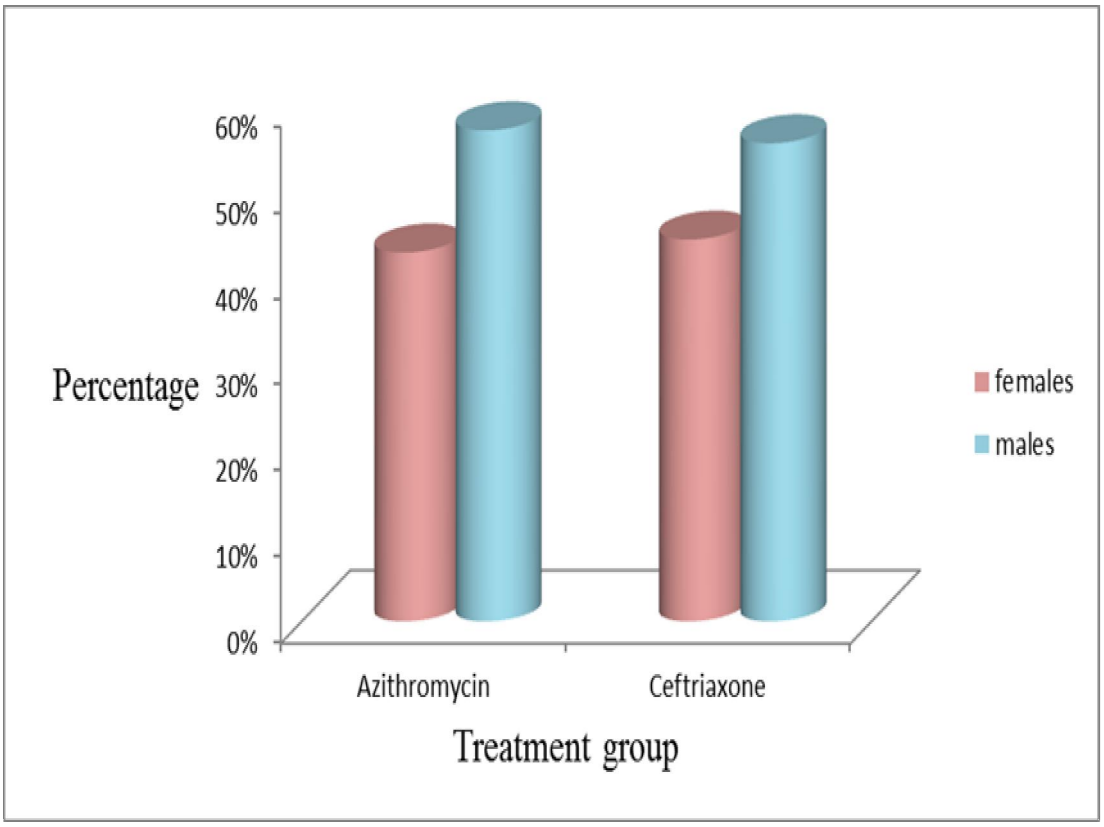
It was observed that 56.3% (n=71) of the total children were boys and 43.6% (n=55) were girls.

Figure 3: Gender distribution (n=126)



Out of the 63 cases 57% (n=36) were boys and 43% (n=27) were girls in the Azithromycin group whereas there were 56% (n=35) boys and 44% (n=28) girls in the Ceftriaxone group.

Figure 4: Gender distribution (Azithromycin vs Ceftriaxone)

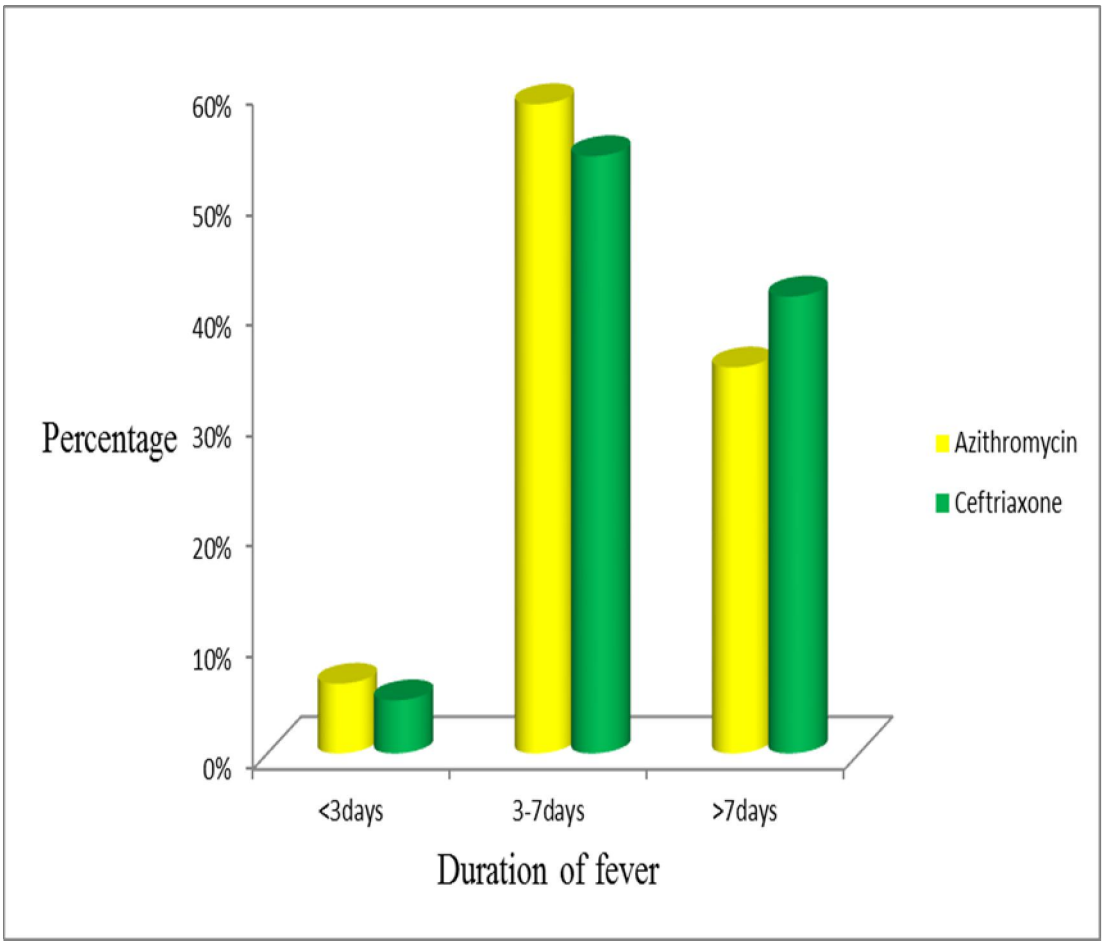


Duration of fever at admission:

It was observed that the mean duration of fever among all children, at the time of admission was 7.66±3.39 days and it was predominantly intermittent type of fever, being associated with chills and rigors in 44.44% (n=56) of the cases. In the Azithromycin group it was 7.4±2.95 days and in the Ceftriaxone group it was 7.92±3.79 days, associated with chills and rigors in 44% (n=28) of cases in both the groups.

In the Azithromycin group, 6% (n=4) cases presented within 3 days of fever, 59% (n=37) cases presented between 3 to 7 days and 35 (n=22) cases presented with fever for more than 7days. In the Ceftriaxone group, 5% (n=3) cases presented with fever for 3 days, 54% (n=34) presented between 3 to 7 days and 41% (n=26) cases had fever for more than 7 days at admission.

Figure 5: Duration of fever at admission (Azithromycin vs Ceftriaxone)



Prior treatment with antibiotics:

History of prior treatment with antibiotics was observed in 27% of total cases (n=34), 32% (n=20) of cases in the Ceftriaxone group and 22% (n=14) of cases in the Azithromycin group.

The antibiotics used were either oral Cephalosporins or Fluoroquinolones.

Epidemiological profile:

In 24.6% (n=31) of the cases, there was history of other family member being affected with typhoid fever at about the same time as the index case. Twenty five percent (n=16) of the cases in Azithromycin group and 24% (n=15) in Ceftriaxone group gave similar history.

In about 12.7% of the total cases there was history of typhoid fever in the neighborhood which was equally distributed (13%) in both groups.

In 14.3% (n=18) of cases, the mother, who used to cook food for the family, had suffered from typhoid fever in the past. In about 18% (n=11) of the cases in the Azithromycin group and 11% (n=7) cases in the Ceftriaxone group, the child's mother had past history of typhoid fever. It was also observed that 12% (n=15) of the total cases had suffered from

typhoid fever in the past which was equally distributed in both the groups (11%).

Among the study group, 13.5% (n=17) of vaccinated cases had developed typhoid, of which 14% (n=9) cases came under Azithromycin group and 13% (n=8) cases under Ceftriaxone group. Vaccine efficacy [calculated by using the formula: {(incidence among unimmunized – incidence among immunized)/incidence among unimmunized} X 100], was observed to be 84.4%.

Table 1: Epidemiological factors

FACTORS		Azithromycin		Ceftriaxone	
		N	%	N	%
Typhoid in other family members		16	25%	15	24%
Typhoid in neighborhood		8	13%	8	13%
Source of drinking water	mineral water	24	38%	18	29%
	metro water	39	62%	45	71%
Boiled water use		15	24%	9	14%
Sanitary latrine	common	27	43%	27	43%
	separate	36	57%	36	57%
Typhoid vaccination		9	14%	8	13%
Eating from vendors		29	46%	27	43%
Past history of typhoid in mother		11	18%	7	11%
Past history of typhoid in child		7	11%	7	11%

Source of drinking water was metro water and mineral water cans in 66.7% (n=84) cases and 33.3% (n=42) cases respectively. About 38% (n=24) cases in Azithromycin group and 29% (n=18) in ceftriaxone group used mineral water for drinking purpose, remaining 62% (n=39) and 71% (n=45) cases used metro water, respectively. Only 19% (n=24) of the total cases, 24% (n=15) cases in the Azithromycin group and 14% (n=9) cases in the Ceftriaxone group consumed water after boiling and cooling.

Sharing toilets with other neighborhood families was observed in 42.9% (n=54) of total cases and in equal proportion of cases in both groups (43%).

About 44.44% (n=56) cases gave history of eating ice creams, chats and other junk food from vendors, out of which 46% (n=29) cases were in Azithromycin group and 43% (n=27) cases in Ceftriaxone group.

Symptomatology:

In the total study population, associated symptoms in decreasing order of frequency were vomiting (54.8%), anorexia (46%), diarrhea (40.5%),abdominal pain (31.7%), cough (25.4%),headache (19%), myalgia (14.3%), loss of weight (5.6%) and constipation (4.8%),

The predominant symptom associated was vomiting (54%, n=34) followed by anorexia (51%, n=32) and diarrhea (38%, n=24) in Azithromycin group, where as in the Ceftriaxone group, anorexia (57%, n=36) was the most common symptom associated, followed by vomiting (56%, n=35) and diarrhea (43%, n=27).

Abdominal pain was seen more commonly in the Ceftriaxone group (37%, n=23) when compared to other treatment group (27%, n=17). But cough was more common in the Azithromycin group (29%, n=18) when compared to Ceftriaxone group (22%, n=14).

Figure 6: Symptomatology (Azithromycin vs Ceftriaxone)

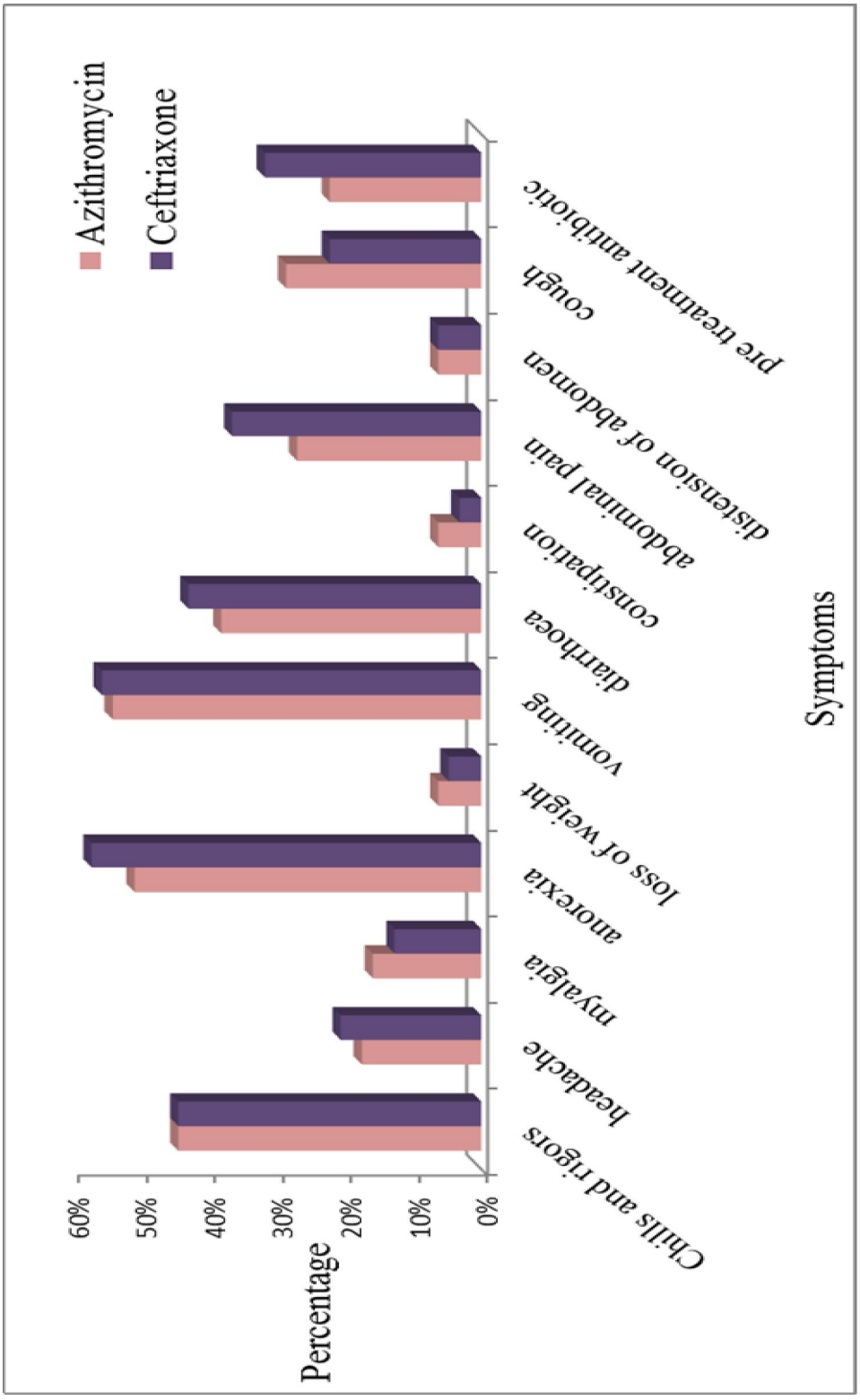


Table 2: Symptomatology

SYMPTOM	Azithromycin	Ceftriaxone
	N = 63	N = 63
Chills and rigors	28	28
Headache	11	13
Myalgia	10	8
Anorexia	32	36
Weight loss	4	3
Vomiting	34	35
Diarrhea	24	27
Constipation	4	2
Abdominal pain	17	23
Abdominal distension	4	4
Cough	18	14
Pretreatment antibiotic use	14	20

Clinical signs:

On examination, the predominant sign observed in the study population was hepatomegaly seen in 92.9% (n=117) cases, followed by coated tongue, glossitis and cheilitis in 67.5% (n=85) cases, splenomegaly in 57.1% (n=72) cases and toxemia in 55.6% (n=70) cases. Other signs observed, in decreasing order of frequency were pallor (52.4%, n=66), abdominal tenderness (19%, n=24), lymphadenopathy (14.3%, n=18), abdominal distension (11.1%, n=14) and rose spots (0.8%, n=1). It was the cervical group of lymph nodes which were predominantly enlarged.

The most common sign elicited in both the groups was hepatomegaly, seen in 94% (n=59) and 92% (n=58) cases in Azithromycin and Ceftriaxone group respectively followed by coated tongue, glossitis and cheilitis in 68% (n=43) cases in Azithromycin group and 67% (n=42) cases in Ceftriaxone group. Splenomegaly was seen in equal proportions in both the groups in about 57% (n=36) cases.

Figure 7: Clinical signs (Azithromycin vs Ceftriaxone)

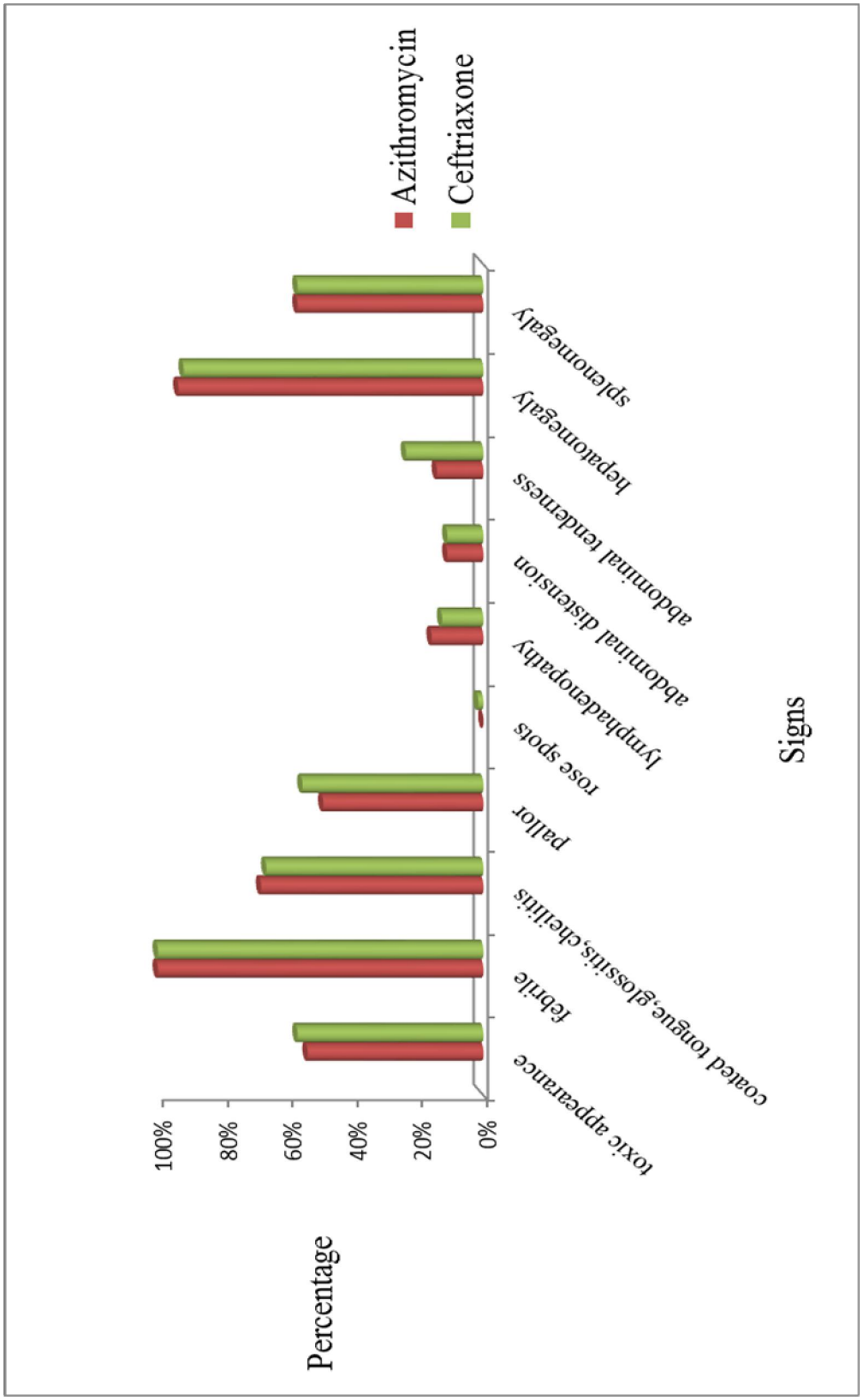


Table 3: Clinical Signs in the study group

SIGN	Azithromycin	Ceftriaxone
	N = 63	**N = 63**
Febrile	63	63
Toxemia	34	36
Coated tongue, glossitis, cheilitis	43	42
Pallor	31	35
Rose spots	0	1
Lymphadenopathy	10	8
Abdominal distension	7	7
Abdominal tenderness	9	15
Hepatomegaly	59	58
Splenomegaly	36	36

Other clinical signs elicited in order of decreasing frequency were toxemia (54%), pallor (49%), lymphadenopathy (16%) and tender abdomen (14%) in Azithromycin group whereas in the Ceftriaxone group it was toxemia (57%), pallor (56%), tender abdomen (24%) and lymphadenopathy (13%). Abdominal distension was seen in equal proportions in both the groups in about 11% (n=7) of the cases. Rose spots was seen in only 2% (n=1) of cases in Ceftriaxone group while none in the Azithromycin group had rose spots.

Investigations:

Complete Blood Count:

Total leucocyte count was normal in 85% (n=107) cases, with leukocytosis in 14.3% (n=18) cases and leucopenia in only 0.8% (n=1) cases.

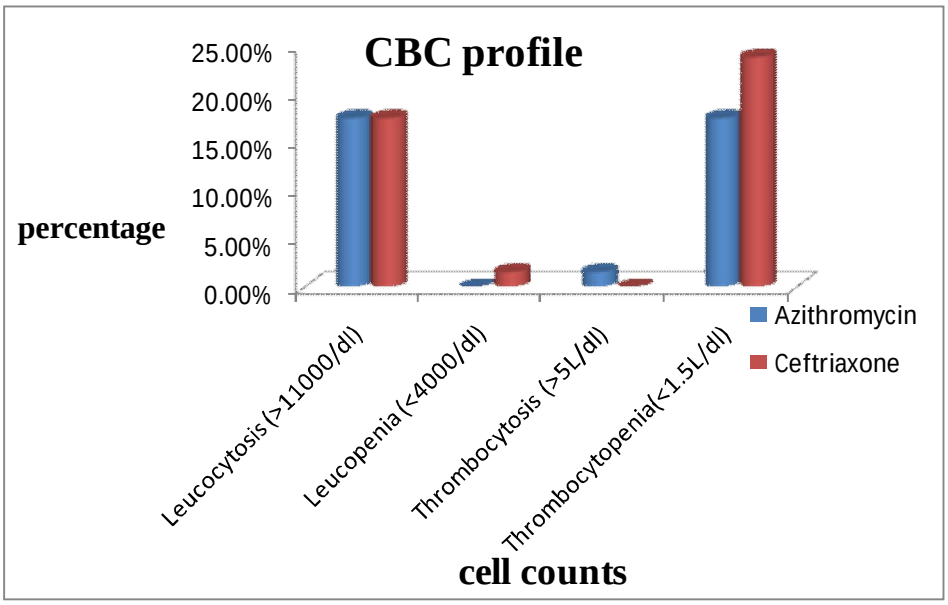
The mean values and SD of hemoglobin, total WBC count with differentials and platelet count in both the treatment groups is listed in Table 7.

Table 4: Complete blood count profile

Parameter	Azithromycin		Ceftriaxone	
	Mean	**SD**	**Mean**	**SD**
Hb	10.88	1.10	10.79	1.17
TLC	7857.14	3363.45	7850.79	2997.20
Neutrophils	52.93	11.72	53.61	13.38
Lymphocytes	37.35	10.15	37.19	11.59
Monocytes	9.16	4.88	8.36	3.50
Eosinophils	0.57	1.02	0.48	1.09
Basophils	0.45	0.35	0.46	0.37
Platelets	2.44	0.94	2.17	0.71

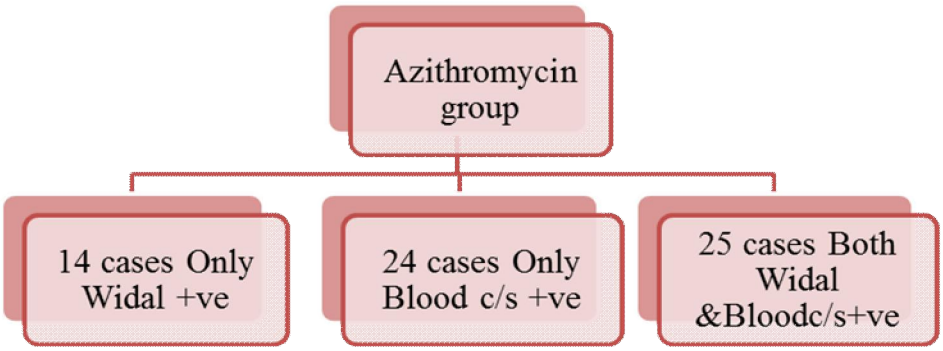
It was observed that leukocytosis (TLC>11,000/dl) was seen in equal proportions (17.5%, n=8) in both groups and leucopenia (TLC<4000/dl) was seen in only 1.6% (n=1) of cases in Ceftriaxone group and none in Azithromycin group. Thrombocytosis (platelet count >5L/dl) was seen in only 1.6% (n=1) of cases in Azithromycin group and none in Ceftriaxone group. Thrombocytopenia (platelet count <1.5L/dl) was observed in 17.5% (n=11) cases in Azithromycin group and 23.8% (n=15) cases in Ceftriaxone group.

Figure 8: CBC profile (Azithromycin vs Ceftriaxone)



CONFIRMATORY TESTS:

Flowchart 1: Confirmatory test positivity (Azithromycin vs Ceftriaxone)



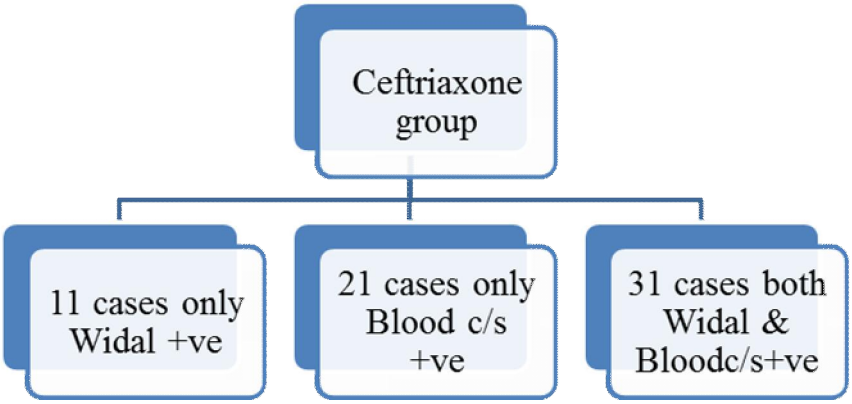
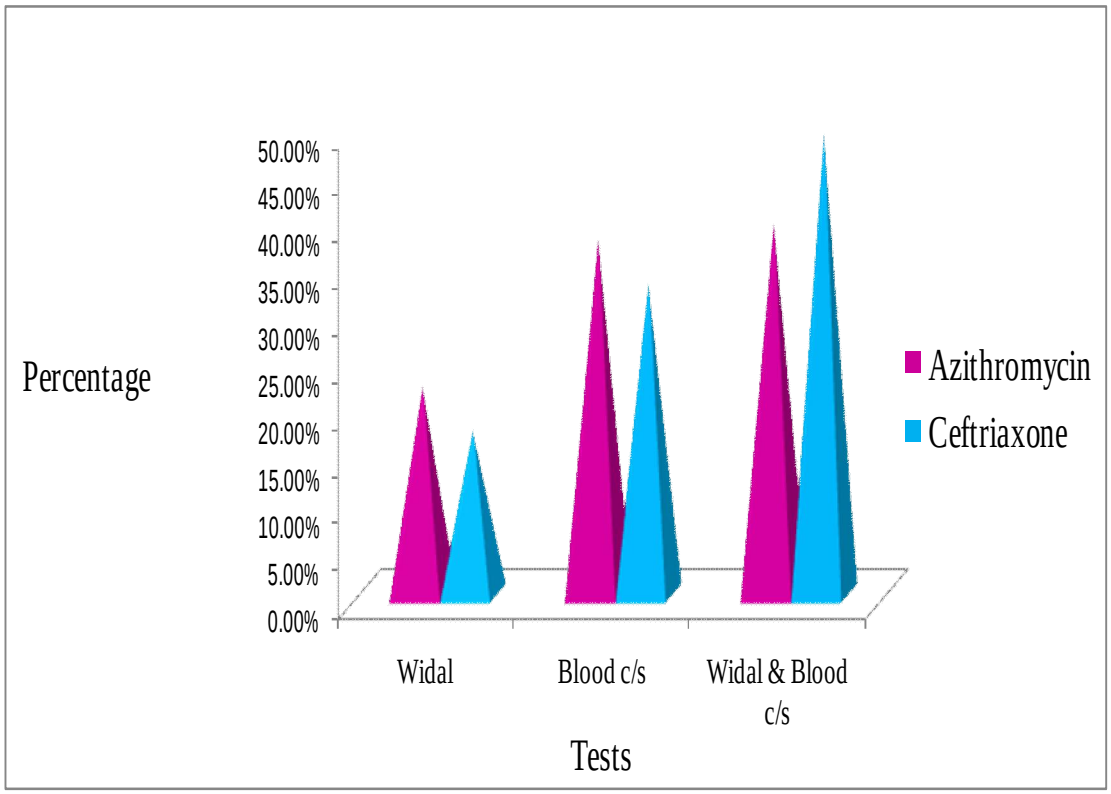


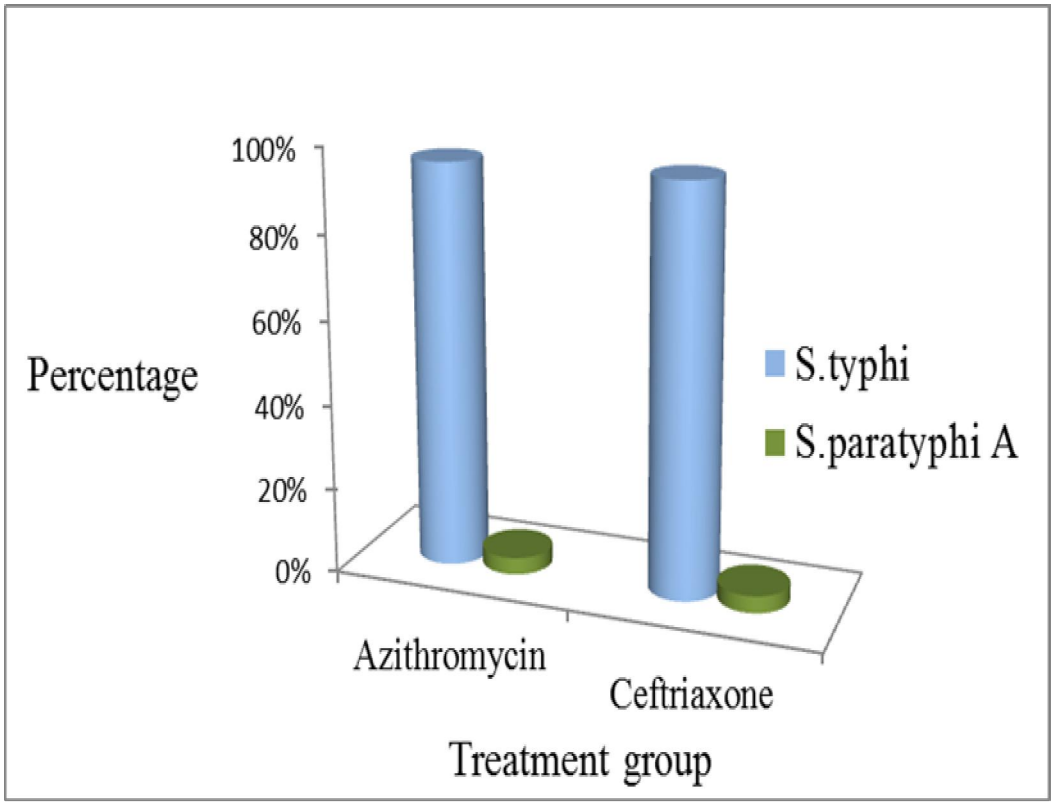
Figure 9: Diagnostic test positivity (Azithromycin vs Ceftriaxone)



Type of Organism Grown:

Among the culture positive cases, 96% cases in both groups grew Salmonella typhi and remaining 4% grew Salmonella paratyphi A.

Figure 10: Type of organism grown in culture (Azithromycin vs Ceftriaxone)



Drug sensitivity and resistance pattern:

Resistance to Nalidixic acid was seen in 42.8% (n=21) of cases in Azithromycin group and 11.5% (n=6) cases in the Ceftriaxone group. Multi drug resistant Salmonella typhi was grown in 6% (n=3) cases in Azithromycin group and in 5.8% (n=3) cases in Ceftriaxone group. Ceftriaxone resistance was observed in 18.4% (n=9) cases in Azithromycin group and in 7.7% (n=4) cases in Ceftriaxone group.

TABLE 5: MDRST, NARST & Ceftriaxone resistance

	Azithromycin	**Ceftriaxone**
Drug resistance	N	N
NARST	21	6
MDRST	3	3
Ceftriaxone resistant	9	4

Figure 11: Drug resistance pattern (Azithromycin vs Ceftriaxone)

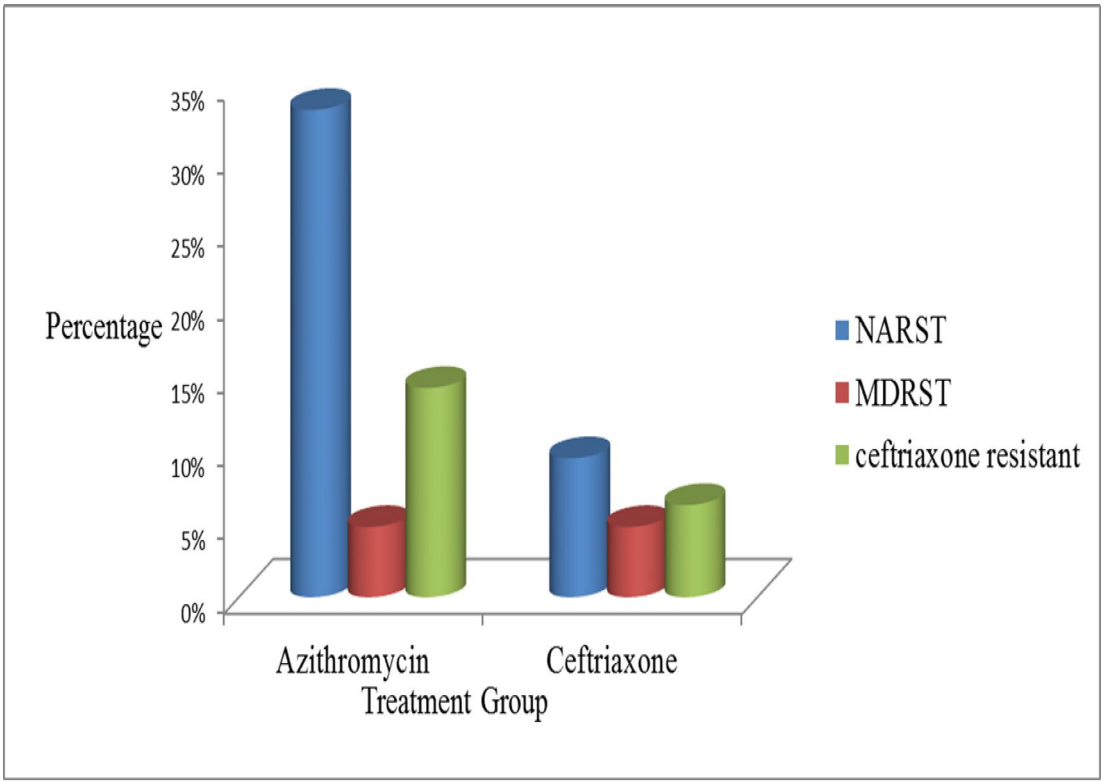


Figure 12: MDRST, NARST and Ceftriaxone resistance (S.typhi vs S.paratyphi)

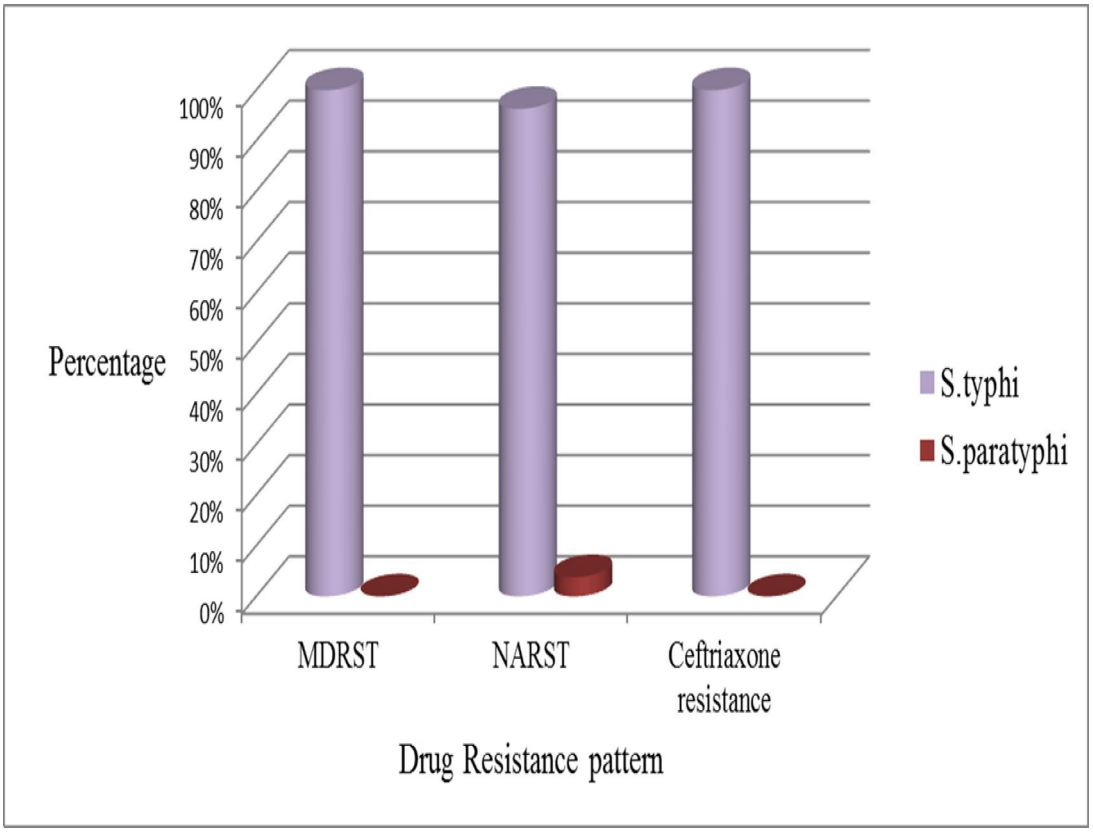


Table 6: MDRST, NARST & Ceftriaxone resistance

Drug resistance	S.typhi	S.paratyphi
(MDRST (N=6)	6	0
NARST (N=27)	26	1
Ceftriaxone resistance (N=13)	13	0

Time taken for diagnosis:

The mean time taken for arriving at the diagnosis in Azithromycin group was 2.89±1.357days and in the Ceftriaxone group was 2.89±1.259 days.

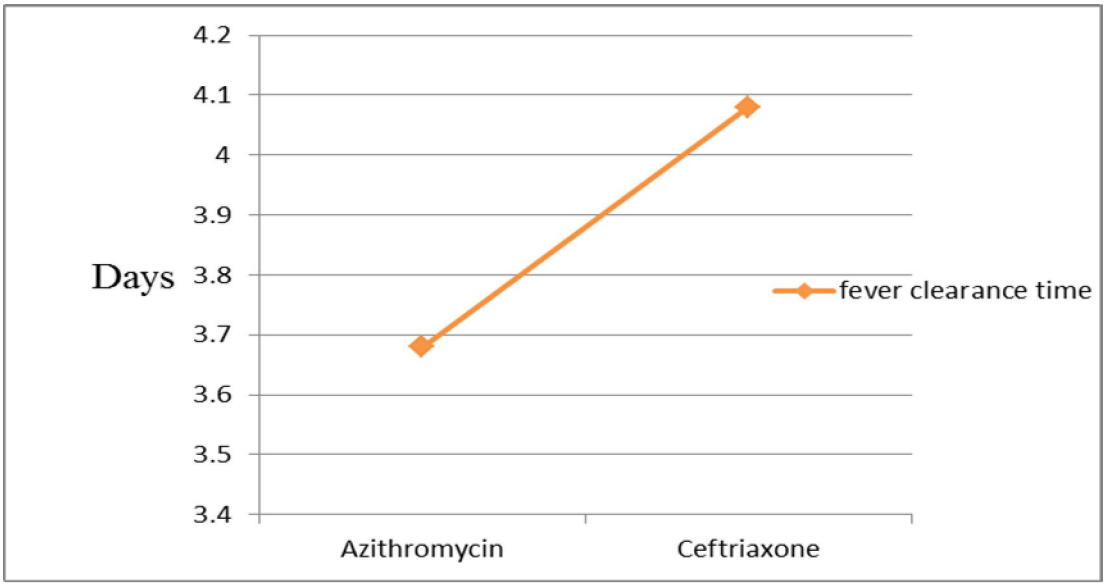
Table 7: Outcome measures - Mean, SD & SE of mean

Descriptive Statistics					
	Groups	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
Duration at diagnosis	Azithromycin	63	2.89	1.357	0.171
	Ceftriaxone	63	2.89	1.259	0.159
Defervescence	Azithromycin	63	3.68	2.109	0.266
	Ceftriaxone	63	4.08	1.903	0.24
Duration of hospital stay	Azithromycin	63	7.35	2.604	0.328
	Ceftriaxone	63	9.44	1.974	0.249
Relapse	Azithromycin	63	0.79	0.408	0.051
	Ceftriaxone	63	0.87	0.421	0.053

Fever clearance time:

The mean fever clearance time in Azithromycin group was 3.68±2.109 days (SE 0.266 and 95% CI) and in Ceftriaxone group was 4.08±1.903 days (SE 0.24 and 95% CI). The p value obtained on comparing the two groups with respect to fever clearance is 0.27.

Figure 13: Mean fever clearance time



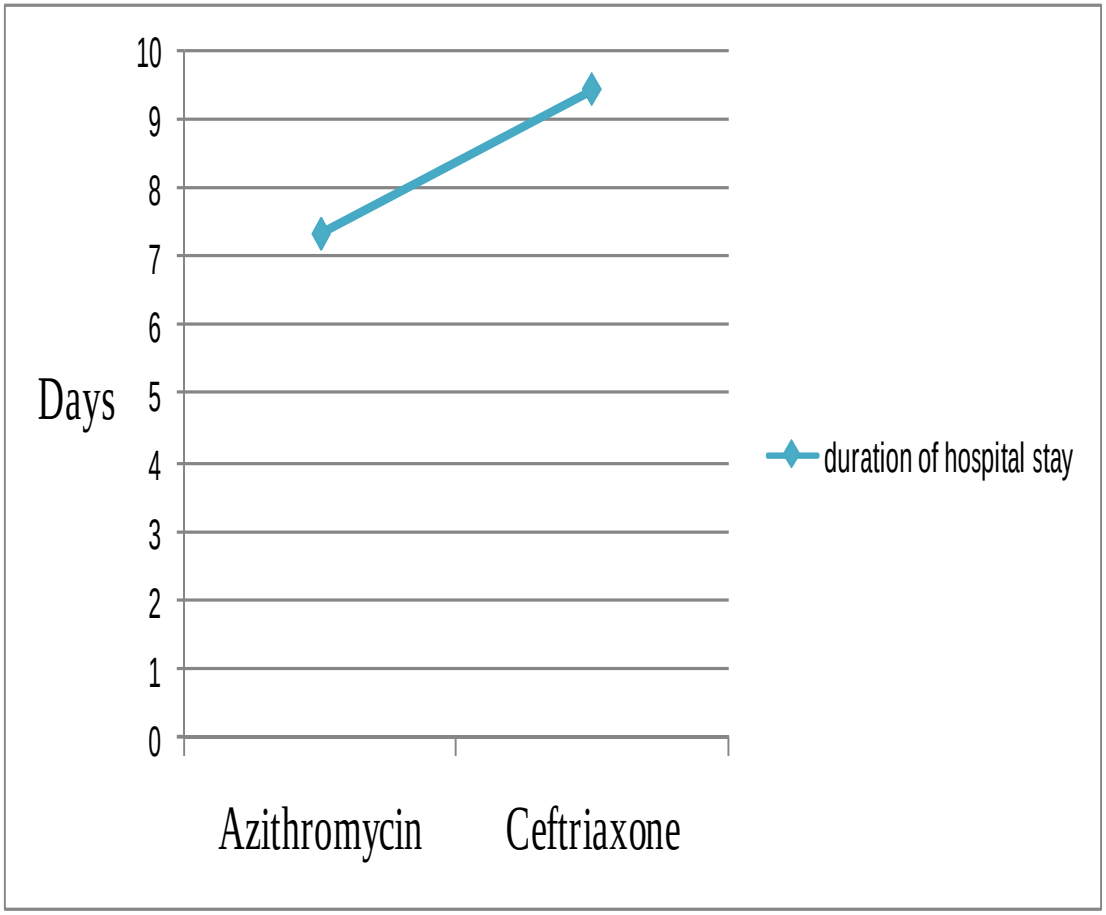
Cross over and treatment failure:

About 4.8% (n=3) cases in Azithromycin group failed to respond to the drug by 7days and hence crossed over to Ceftriaxone group. 6.3% (n=4) cases had delayed response to intra venous Ceftriaxone requiring continuation of the drug for more than 7days till 24-48hrs of defervescence.

Duration of Hospital stay:

The mean duration of hospital stay in the Azithromycin group was7.35±2.604 days (SE 0.328) and in the Ceftriaxone group was 9.44±0.249days (SE 0.249). The p value obtained on comparing the two groups with respect to duration of hospital stay was 0.0001 which is highly significant.

Figure 14: Mean duration of hospital stay



Relapse:

During thirty day follow up, 3.2% (n=2) cases in the Ceftriaxone group had relapsed but there was no relapse in the Azithromycin group. The p value obtained on comparing both the groups with respect to relapse is 0.285 which is statistically insignificant.

Table 8: Independent t test for outcome measures

Independent Samples Test									
Equal variances assumed	**Levene's Test for Equality of Variances**					**t-test for Equality of Means**		**95% C I of the Difference**	
	F test value	**p value**	**t test value**	**Df**	**p value**	**Mean Difference**	**Std. Error Difference**	**Lower**	**Upper**
Duration at diagnosis	1.879	0.173 (NS)	0	124	1 (NS)	0.000	0.233	-0.462	0.462
Defervescence	0.798	0.373 (NS)	-1.109	124	0.27 (NS)	-0.397	0.358	-1.105	0.312
Duration Of hospital stay	1.26	0.264 (NS)	-5.09	124	0.0001***	-2.095	0.412	-2.91	-1.28
Relapse	1.022	0.314 (NS)	-1.075	124	0.285 (NS)	-0.079	0.074	-0.226	0.067

Analysis of Primary Objective:

On applying Null hypothesis that oral Azithromycin is as effective as intra venous Ceftriaxone in the management of uncomplicated Enteric fever, p value obtained with respect to fever defervescence was 0.27. Hence Null hypothesis not rejected. It means that in 27% of the study group, Azithromycin is as effective as Ceftriaxone. But in the remaining 73%, Azithromycin is not as effective as Ceftriaxone.

On calculating the mean difference for fever clearance in both the groups it was -0.397 i.e. the time taken for fever clearance in Azithromycin group was lesser than that in the other group. It implies that Oral Azithromycin may be more effective than intra venous Ceftriaxone (A>C). But because the study sample was small, this inference is not statistically significant.

Flow chart 2: Patient enrollment and follow up

DISCUSSION

DISCUSSION

Typhoid fever accounts for significant morbidity among children in our country. It is not just the morbidity of the illness alone but also the socioeconomic burden which has important implications in the effective management of the disease. Financial constraints are encountered, not only by the expenses of hospital admission for IV antibiotics but also by the loss of wages of working parents. The recent upsurge in MDRST and NARST is a rising concern to the managing physician and has prompted further clinical trials to search for newer, cheaper and orally available drugs.

In our study an attempt was made to test the efficacy of an orally available drug namely Azithromycin in treating enteric fever as compared to the classically administered injectable Ceftriaxone. Besides we also studied the clinical, laboratory and epidemiological profile of these cases with a view to find out whether any of these factors could predict the occurrence of the disease or make a difference to the outcome after treatment. A total of 126 children with uncomplicated enteric fever were grouped into two groups; one received Azithromycin, the other Ceftriaxone. Both groups were compared with regard to efficacy.

The mean age of the participants in our study group was 7years, with 44.4% in the age group of 2-6years and 55.6% between 7-12years (Figures 1 & 2). The rising typhoid incidence in younger age noted in our study is related to improper sanitation and due to the fact that younger children are unaware of heath hygiene. The male: female ratio was 1.29:1in our study (Figures 3 & 4), which was similar to that seen in the study by Ganesh et al. [14] The predominant clinical profile (Table 2 & 3; Figures 5, 6 & 7) observed in our study was fever associated with vomiting, anorexia, diarrhea and hepatosplenomegaly, which was similar to that reported in other studies. [14, 28, 29]

Mary Mallon, a cook, was described as 'the most dangerous lady of the United States', for the epidemics of typhoid she had caused as a chronic carrier. In about 14.3% of the cases in our study, the mother who used to cook food for the family had suffered from typhoid fever in the past (Table 1). History of typhoid fever in other family members was seen in 24.6% of cases as compared to 6% observed by Ram et al.[18] This fact calls for a strong recommendation for testing carrier state in adult typhoid patients following cure. [2, 18]

They also observed that almost 90% of the cases in their study used unboiled drinking water as against 81% cases in our study, thus highlighting the need for boiling water as part of food safety. [18]

They found a statistically significant association between use of sanitary latrines for defecation and the occurrence of typhoid fever. They had concluded that the use of sanitary latrines was protective against acquiring the infection. In our study 100% of the cases used sanitary latrine for defecation and about 43% of the cases shared toilet facilities with other families, thereby compromising health hygiene.[18]

Though enteric fever is classical known to have leucopenia, in our study 85% cases had normal total count with leucopenia observed only in one case and leukocytosis in 14.3% (n=18) cases (Figure 8). This was in agreement with Ganesh et al[14] study, though they had observed a lesser percentage of cases with leukocytosis.

The global increase in the emergence of resistant strains among salmonella typhi is well documented. In our study NARST accounted for 21.4%, MDRST for 4.8% and Ceftriaxone resistance in10.3% of cases. Out of the 21.4% cases of NARST, 0.8% of S.paratyphi and 20.6% of S.typhi were Nalidixic acid resistant strains (Table 5 & 6; Figure 11 & 12). None of the paratyphi strains were MDRST nor resistant to Ceftriaxone. The occurrence of resistance was much lower when compared with Walia et al[28] study, wherein they have noted 76.7% and 74.3% cases of NARST in the S.paratyphi and S.typhi groups respectively. MDRST observed in their study was 19.7% cases in S.typhi group and none in paratyphi group. They had no cases of Ceftriaxone

resistance in their study. Our hospital caters to the ESI beneficiaries for whom, under the social security scheme, holistic medical care is given with minimum individual contribution. Hence the parents directly come to us seeking medical attention for febrile illness in their children. Thus protection is offered against indiscriminate antibiotic use since drugs are started only after some confirmatory evidence, except in emergencies. A much lower percentage of MDRST in our series is an indirect proof against antibiotic abuse. The emerging drug resistance to Ceftriaxone seen in our series is probably related to the fact that before undertaking this study Ceftriaxone was given being used as the sole drug for all cases of proved enteric fever.

In their retrospective analysis of cases spread over 2 years, Ganesh et al[14] observed that NARST had increased from 56% in the first year to 73% in the second year, probably again related to the surging antibiotic abuse.

Comparison of relative efficacy of Azithromycin and Ceftriaxone was done in terms of fever defervescence, duration of hospital stay and relapse (Table 7 & 8; Figures 13 & 14). The mean fever clearance time in Azithromycin group was 3.68±2.109 days and in Ceftriaxone group was 4.08±1.903 days. The earlier fever defervescence seen with Azithromycin marks its potential as a promising oral alternative. This inference though statistically not significant, because of the small number, paves the way

for larger studies in future. The difference in defervescence pattern with the use of both the drugs in our study is however contrary to that observed by Frenck et al[27] wherein they had observed early defervescence with Ceftriaxone rather than with Azithromycin. The emerging resistance over the last 10 years has probably caused the change in fever defervescence pattern with the usage of both the drugs.

Gupta et al[29] had noted a fever clearance time of 4.3days with Ceftriaxone. In other noncomparative studies where only Azithromycin was used, such as those done by Anju et al[20] and Hussain et al[22], the mean duration of defervescence was 3.45±1.92 days and 4days respectively. These observations concurred with our findings.

The mean duration of hospital stay in the Azithromycin group was 7.35±2.604 days and in the Ceftriaxone group were 9.44±0.249 days. The p value obtained on comparing the two groups with respect to duration of hospital stay was 0.0001 which was highly significant. Implying that oral Azithromycin significantly reduces the duration of hospital stay when compared to intra venous Ceftriaxone. Thus with the use of Azithromycin, there is a convenience of early discharge soon after fever and toxemia clears as the course can be completed even at home. In nontoxic cases there remains an option of using the drug even on outpatient basis thus making it a better alternative.

In enteric fever, there always remains a potential risk of relapse following even effective treatment. About 3.2% (n=2) cases treated with Ceftriaxone relapsed within 4 weeks of treatment, which was lesser when compared to that observed by Bhutta et al[30], Parry et al[24] and Dutta et al[31] (5-10%) and Frenck et al[27] (19%) in their studies. Azithromycin group did not have any relapse, which was similar to that seen in studies by Frenck et al[27], Anju et al[20] and Hussain et al.[22] Use of Azithromycin seems to have some protection against relapses which can be considered as a definite advantage.

Out of the four cases that had delayed response to intra venous Ceftriaxone, one was resistant to Ceftriaxone but ultimately responded. Two cases relapsed and one case neither had resistance to Ceftriaxone nor relapsed.

The dreaded complication of asymptomatic carrier state following enteric fever is more of adult concern and children are sort of protected from this state. This is also seen in our study wherein none of the children in both the groups had a positive fecal culture during the 4 weeks follow up, which was similar to the observation made by Frenck et al.[27]

Vaccine efficacy in our series was 84.4%, as against 32% observed by Ganesh et al in their study.[14] Since preliminary analysis showed that vaccine administration offered a significant protection against the disease, we in our hospital have started this immunization for pediatric patients on

a trial basis and are attempting to compare the incidence of enteric fever in the next few years as compared to the pre vaccination era.

Thus in our study oral Azithromycin was found to be as effective as intravenous Ceftriaxone in terms of fever defervescence, duration of hospital stay and prevention of relapse though larger studies are required for validating. Being an oral drug, it markedly reduces the admission expenditure as well as prevents loss of wages for working parents thus reducing the overall socio economic burden.

CONCLUSION

CONCLUSION

1. With regards to the primary objective, we found in our study that Oral Azithromycin is as effective as intravenous Ceftriaxone in treating typhoid fever. Though the time taken for fever clearance was not statistically significant between the two treatment groups, Azithromycin has a slightly earlier fever clearance than Ceftriaxone with no relapse.

2. Being an oral drug, it does significantly reduce the duration of hospitalization, thereby reducing the loss of working days for the child’s parents and finally reducing the socioeconomic burden to some extent.

LIMITATIONS

LIMITATIONS

1. The sample size in our study was small. Hence further studies are needed to validate these results.

2. Demonstration of microbiological response or failure, by repeating culture at 1 week could not be done due to resource constraints.

3. The relative efficacy of the drugs was determined purely on clinical grounds. Minimum inhibitory concentrations of the drugs could not be estimated due to resource constraints.

4. There was no blinding in our study.

RECOMMENDATIONS

RECOMMENDATIONS

1. Oral Azithromycin can be used in place of intravenous Ceftriaxone in the management of uncomplicated Enteric fever to reduce time taken for fever defervescence, duration of hospital stay and to prevent relapse.

2. Management of every case of Enteric fever should be holistic, addressing not only the acute illness, but also the risk factors by providing effective health education and promoting environmental hygiene.

3. Adult households must be screened for chronic carrier state.

4. Prevention is always better than cure; hence vaccination against typhoid fever must be propagated and practiced effectively to reduce the National and Global burden of the disease.

ANNEXURE - IV

MASTER CHART

Name	age	sex	duration of fever	pattern of fever	chills and rigors	headache	myalgia	altered sensorium	seizures	anorexia	loss of weight	vomiting	diarrhoea	constipation	abdominal pain	distension of abdominal	cough	breathlessness	prior treatment with antibiotics	toxic look	febrile
surya	11	M	10	intermittent	A	A	A	A	A	P	A	P	A	A	A	A	A	A	Y	A	P
Chandralekha	2	F	5	intermittent	P	A	A	A	A	P	A	A	P	A	A	A	A	A	N	P	P
Abhinaya	10	F	9	intermittent	A	A	A	A	A	A	A	P	P	A	P	A	A	A	N	P	P
Sajani	2	F	7	intermittent	A	A	A	A	A	A	P	P	A	P	A	A	A	A	N	P	P
Pawan kumar	2	M	6	intermittent	A	A	A	A	A	P	A	A	A	A	A	A	A	A	N	P	P
Adhira krishnan	8	F	7	intermittent	P	A	A	A	A	A	A	A	A	A	P	A	A	A	N	P	P
Narendar	5	M	5	intermittent	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	A	P
sabir basha	10	M	9	intermittent	P	A	A	A	A	P	A	P	A	A	P	A	A	A	N	P	P
vijaya kumar	6	M	15	intermittent	P	A	A	A	A	P	A	A	A	A	P	A	P	A	Y	A	P
jayashree	7	F	7	intermittent	P	A	A	A	A	A	A	P	A	A	P	A	P	A	N	A	P
vignesh	4	M	4	intermittent	P	A	A	A	A	A	A	P	P	A	A	P	A	A	N	P	P
sabari	4	M	4	intermittent	P	A	A	A	A	P	P	A	A	A	A	A	A	A	N	A	P
praveen kumar	7	M	10	intermittent	P	P	A	A	A	P	A	A	A	A	A	A	A	A	N	A	P
Rohith	6	M	7	intermittent	P	P	A	A	A	A	A	A	A	A	A	A	P	A	Y	A	P
Kabilan	10	M	10	intermittent	P	P	P	A	A	A	P	A	P	A	P	A	A	A	Y	P	P
manimegalai	12	F	7	intermittent		P	P	P	A	P	A	P	A	A	A	A	P	A	N	A	P
subburam	8	M	5	intermittent	P	A	A	A	A	A	A	A	A	A	A	A	A	A	N	A	P
sanjay	9	M	8	intermittent	P	A	A	A	A	P	A	P	P	A	A	A	A	A	N	P	P
sofia rani	4	F	10	intermittent	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Y	A	P
Nithyashree	11	F	14	intermittent	P	A	A	A	A	P	A	A	A	A	A	A	A	A	N	P	P
Karthik	11	M	7	intermittent	A	A	A	A	A	A	A	P	P	A	P	A	A	A	N	A	P
Manoranjitham	3	F	6	intermittent	A	A	A	A	A	P	A	A	A	A	P	A	A	A	N	P	P
prashanth	11	M	17	intermittent	A	A	A	A	A	P	P	P	A	A	A	A	P	A	Y	P	P
Karthiga	6	F	10	intermittent	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	A	P
Balavignesh	8	M	7	intermittent	A	A	P	A	A	A	A	A	A	A	A	A	P	A	N	A	P
Amith kumar	4	M	8	intermittent	P	A	A	A	A	A	A	A	A	P	A	A	P	A	N	P	P
rakesh	6	M	7	intermittent	P	A	P	A	A	P	A	P	A	P	A	A	P	A	N	P	P
yuvashree	7	F	5	intermittent	P	A	A	A	A	P	A	P	A	A	A	A	P	A	N	P	P
john	4	M	7	intermittent	A	A	A	A	A	A	A	A	A	A	P	A	A	A	N	P	P
renuka	9	F	8	intermittent	P	A	A	A	A	P	A	P	P	A	A	A	A	A	N	P	P
dhanesh	11	M	5	remittent	A	A	A	A	A	P	A	P	P	A	A	A	P	A	N	P	P
yuvraj	8	M	3	intermittent	A	A	A	A	A	P	A	P	P	A	A	A	P	A	N	A	P
mahendran	11	M	10	intermittent	P	A	P	A	A	P	A	P	P	A	A	A	A	A	Y	P	P
hemavathi	7	F	6	intermittent	P	A	P	A	A	P	A	A	A	A	A	A	P	A	N	P	P
priscilla	6	F	8	intermittent	A	A	A	A	A	P	A	P	P	A	A	A	A	A	N	A	P
sadik	8	M	7	intermittent	P	A	P	A	A	P	A	A	A	A	A	A	P	A	Y	A	P
dhanyashri	11	F	7	intermittent	A	A	A	A	A	P	A	A	A	A	A	A	A	A	N	A	P
Gayathri devi	10	F	7	intermittent	P	P	P	A	A	A	A	A	A	A	A	A	P	A	Y	P	P
ramakrishnan	7	M	7	intermittent	A	A	A	A	A	A	A	A	A	A	A	A	P	A	N	A	P
visakan	12	M	7	intermittent	P	P	A	A	A	A	A	P	A	A	A	P	A	A	N	A	P
Roseline	11	F	7	intermittent	A	P	A	A	A	P	A	A	A	P	A	A	A	A	N	A	P
Dashwanth	4	M	5	intermittent	A	P	A	A	A	A	A	P	A	A	A	A	P	A	Y	A	P
harikrishnan	8	M	4	intermittent	A	A	A	A	A	A	A	A	P	A	P	A	P	A	N	A	P
deepika	11	F	15	intermittent	P	A	A	A	A	A	A	P	A	A	P	A	A	A	N	A	P
devanandhan	10	M	3	intermittent	P	P	A	A	A	A	A	P	P	A	A	A	A	A	N	A	P
dharanitharan	6	M	7	intermittent	P	A	P	A	A	P	A	P	A	A	A	A	A	A	N	P	P
Abhinaya	8	F	10	intermittent	P	A	A	A	A	A	A	A	P	A	A	P	A	A	N	A	P
emancy	2	F	13	intermittent	A	A	A	A	A	A	A	P	P	A	A	A	A	A	Y	A	P
gomathi	9	F	4	intermittent	A	A	A	A	A	A	A	P	P	A	P	A	A	A	N	P	P
hemavathi	8	F	8	intermittent	A	A	A	A	A	P	A	P	A	A	A	A	A	A	Y	P	P
mahesh	2	M	4	intermittent	A	A	A	A	A	P	A	P	P	A	A	A	A	A	N	P	P
ramesh	2	M	3	intermittent	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Y	A	P
dharun	8	M	8	intermittent	P	A	A	A	A	A	A	A	P	A	A	A	A	A	N	P	P
dhanesh	10	M	3	intermittent	A	P	A	A	A	A	A	P	P	A	P	A	A	A	N	P	P
sarath	10	M	7	intermittent	A	P	P	A	A	A	A	P	A	A	A	A	A	A	N	P	P
devesh	9	F	7	intermittent	A	A	A	A	A	P	A	P	P	A	P	A	A	A	N	P	P
keerthi	12	F	7	intermittent	A	A	A	A	A	P	A	P	P	A	P	A	P	A	N	P	P
sameera banu	2	F	5	intermittent	A	A	A	A	A	A	A	P	A	A	P	P	A	A	N	P	P
krithi	6	F	8	intermittent	A	A	A	A	A	P	A	P	P	A	A	A	A	A	Y	P	P
ranjith	2	M	7	intermittent	A	A	A	A	A	P	A	A	P	A	A	A	A	A	N	A	P
preethi	2	F	11	intermittent	A	A	A	A	A	A	A	P	A	A	A	A	A	A	N	P	P
vignesh	2	M	5	intermittent	A	A	A	A	A	P	A	A	A	A	A	A	A	A	N	A	P
pranesh	12	M	7	intermittent	A	A	A	A	A	A	A	P	P	A	P	A	A	A	N	P	P

Name	coated tongue, glossitis, cheilitis	pallor	icterus	rose spots	lymphadenopathy	abdominal distension	abdominal tenderness	hepatomegaly	splenomegaly	complications	other family member affection	typhoid in neighbourhood	source of drinking water	boiled water	sanitary latrine	typhoid vaccination	eating from vendors	past history of typhoid in mother	past history of typhoid in index child	treatment	duration of treatment	defervescence	duration of hospital stay	duration at diagnosis	Hb
surya	P	A	A	A	A	A	P	P	A	A	N	N	Metro water	N	Separate	N	Y	N	N	zithromyci	7days	2days	5days	2days	11.3
Chandralekha	P	P	A	A	A	A	A	P	P	A	N	N	Metro water	N	Separate	N	N	N	N	zithromyci	7days	5days	10days	5days	10
Abhinaya	P	A	A	A	A	A	A	P	P	A	N	Y	Metro water	N	Separate	N	N	N	N	zithromyci	7days	2days	6days	2days	11.6
Sajani	P	P	A	A	A	P	A	P	P	A	N	N	Metro water	N	Separate	N	N	N	N	zithromyci	7days	5days	7days	2days	9.5
Pawan kumar	P	P	A	A	A	A	A	P	A	A	N	N	Metro water	N	Separate	N	N	N	N	zithromyci	7days	2days	6days	2days	10
Adhira krishnan	P	A	A	A	A	A	A	P	A	A	N	N	Metro water	N	Separate	N	N	N	N	zithromyci	7days	3days	6days	1day	11
Narendar	P	P	A	A	P	A	A	P	P	A	N	N	Mineral water	N	Separate	Y	N	N	N	zithromyci	7days	6days	10days	2days	10.6
sabir basha	P	A	A	A	A	A	A	P	P	A	Y	N	Metro water	N	common	N	Y	Y	Y	zithromyci	7days	5days	7days	1day	12
vijaya kumar	A	P	A	A	P	A	A	P	A	A	N	N	Metro water	N	common	N	N	Y	N	zithromyci	7days	2days	7days	4days	10.2
jayashree	A	A	A	A	P	A	P	P	P	A	N	N	Mineral water	N	common	N	N	N	N	zithromyci	7days	5days	10days	3days	11.6
vignesh	P	P	A	A	P	A	A	P	A	A	N	N	Metro water	Y	Separate	N	Y	N	N	ays and ce	15days	12days	17days	6days	8.1
sabari	A	P	A	A	A	A	P	P	P	A	Y	N	Metro water	N	Separate	N	N	N	N	zithromyci	7days	2days	7days	4days	10.9
praveen kumar	P	P	A	A	A	A	A	P	P	A	N	N	Metro water	Y	common	N	N	N	N	zithromyci	7days	2days	5days	2days	11
Rohith	A	A	A	A	A	A	A	P	A	A	Y	N	Metro water	N	Separate	N	Y	Y	N	zithromyci	7days	2days	5days	2days	11.1
Kabilan	P	A	A	A	A	A	A	P	P	A	N	N	Mineral water	N	Separate	N	N	N	N	zithromyci	7days	2days	2days	5days	11.9
manimegalai	A	A	A	A	A	A	A	P	A	A	Y	N	Metro water	Y	common	N	Y	N	Y	zithromyci	7days	4days	7days	2days	13
subburam	A	A	A	A	P	A	A	P	A	A	N	N	Metro water	N	common	N	Y	N	N	zithromyci	7days	2days	5days	2days	12.5
sanjay	P	A	A	A	A	A	A	P	A	A	N	N	Metro water	Y	Separate	N	N	N	N	zithromyci	7days	2days	7days	3days	10.8
sofia rani	P	P	A	A	A	A	A	P	A	A	N	N	Mineral water	N	common	N	Y	N	N	zithromyci	6days	8days	15days	2days	10.8
Nithyashree	P	A	A	A	A	A	A	P	A	A	N	N	Metro water	N	common	N	Y	N	N	zithromyci	7days	2days	4days	1day	11.1
Karthik	P	A	A	A	A	A	A	P	A	A	N	N	Mineral water	N	Separate	N	N	N	N	zithromyci	7days	2days	7days	4days	11.5
Manoranjitham	P	A	A	A	A	A	A	P	A	A	Y	N	Mineral water	N	common	N	N	N	N	zithromyci	7days	4days	10days	5days	11.1
prashanth	P	A	A	A	A	A	A	P	A	A	N	N	Metro water	Y	Separate	N	N	Y	N	zithromyci	7days	3days	5days	1day	11.6
Karthiga	A	A	A	A	A	A	A	P	P	A	Y	N	Mineral water	N	common	Y	N	N	Y	zithromyci	7days	5days	6days	1day	11.6
Balavignesh	P	P	A	A	A	A	A	P	P	A	N	N	Metro water	N	common	N	N	N	N	zithromyci	7days	2days	7days	5days	10.1
Amith kumar	P	A	A	A	A	A	A	P	P	A	N	Y	Mineral water	N	common	N	Y	N	N	zithromyci	7days	3days	7days	4days	8.3
rakesh	P	A	A	A	A	A	A	P	P	A	N	Y	Metro water	N	common	N	N	N	N	zithromyci	7days	6days	7days	2days	11.1
yuvashree	P	A	A	A	A	A	A	P	p	A	N	N	Metro water	N	common	N	Y	Y	N	zithromyci	7days	3days	8days	4days	11.3
john	P	P	A	A	A	A	A	P	P	A	Y	N	Mineral water	N	Separate	N	N	N	N	zithromyci	7days	7days	9days	1day	10.3
renuka	P	P	A	A	P	A	A	P	P	A	Y	N	Mineral water	N	Separate	Y	Y	N	N	zithromyci	7days	2days	6days	3days	11
dhanesh	P	A	A	A	A	A	A	P	A	A	Y	N	Mineral water	N	Separate	N	Y	N	N	zithromyci	7days	6days	9days	3days	12.2
yuvraj	P	P	A	A	A	A	A	P	P	A	N	N	Metro water	N	Separate	N	Y	N	N	zithromyci	7days	3days	8days	4days	10.6
mahendran	P	P	A	A	A	A	A	P	P	A	N	N	Metro water	N	common	N	Y	N	N	zithromyci	7days	4days	10days	5days	11.4
hemavathi	P	P	A	A	A	P	A	P	P	A	N	N	Metro water	Y	Separate	N	Y	N	N	zithromyci	7days	3days	7days	2days	11.4
priscilla	A	P	A	A	A	A	A	P	A	A	N	N	Mineral water	Y	Separate	Y	Y	Y	N	zithromyci	7days	4days	8days	3days	11.6
sadik	A	P	A	A	P	A	P	P	P	A	N	N	Metro water	N	common	N	Y	N	Y	zithromyci	7days	6days	11days	4days	11.4
dhanyashri	A	P	A	A	A	A	A	P	A	A	N	N	Mineral water	N	Separate	N	N	N	N	zithromyci	7days	2days	4days	1day	10
Gayathri devi	A	P	A	A	A	A	A	A	A	A	N	Y	Mineral water	N	Separate	Y	Y	N	N	zithromyci	7days	3days	8days	4days	9.6
ramakrishnan	P	P	A	A	P	A	A	P	P	A	N	N	Metro water	Y	Separate	N	N	N	N	zithromyci	7days	2days	4days	1day	9.8
visakan	A	A	A	A	A	A	P	P	A	A	Y	N	Mineral water	N	common	N	Y	N	N	zithromyci	7days	2days	8days	4days	14.2
Roseline	P	A	A	A	A	A	A	P	P	A	N	Y	Metro water	N	common	N	Y	N	N	zithromyci	7days	2days	4days	1day	11.6
Dashwanth	P	P	A	A	A	A	A	A	A	A	Y	Y	Mineral water	N	Separate	N	Y	Y	N	zithromyci	7days	2days	5days	2days	8.8
harikrishnan	A	A	A	A	A	A	A	P	P	A	Y	N	Metro water	N	Separate	N	N	N	Y	zithromyci	7days	2days	7days	4days	11.3
deepika	P	P	A	A	A	A	A	P	P	A	N	N	Metro water	N	Separate	N	Y	N	N	zithromyci	7days	5days	7days	1day	10.3
devanandhan	A	A	A	A	A	A	A	A	A	A	N	N	Metro water	Y	common	N	Y	Y	N	zithromyci	7days	4days	9days	4days	11.2
dharanitharan	P	P	A	A	A	A	A	P	P	A	N	Y	Mineral water	Y	common	N	N	N	N	zithromyci	7days	4days	9days	2days	9.9
Abhinaya	P	A	A	A	P	P	A	P	A	A	N	N	Mineral water	Y	Separate	Y	Y	Y	N	zithromyci	7days	3days	7days	4days	12.2
emancy	A	P	A	A	A	P	A	P	P	A	Y	Y	Mineral water	Y	Separate	N	N	N	N	zithromyci	7days	2days	7days	3days	9.4
gomathi	A	A	A	A	A	A	P	P	P	A	Y	N	mineral water	N	Separate	Y	Y	N	N	zithromyci	7days	5days	8days	3days	11
hemavathi	P	A	A	A	P	A	A	P	P	A	N	N	metro water	Y	Separate	N	N	Y	N	zithromyci	7days	4days	9days	5days	10.9
mahesh	P	P	A	A	A	A	A	P	A	A	N	N	metro water	Y	Separate	N	N	N	N	zithromyci	7days	3days	5days	2days	9.5
ramesh	A	P	A	A	A	A	A	P	P	A	N	N	mineral water	N	common	N	N	Y	N	zithromyci	7days	3days	7days	4days	10.5
dharun	P	A	A	A	A	A	A	P	A	A	N	N	metro water	N	Separate	N	Y	N	N	zithromyci	7days	3days	7days	4days	12.9
dhanesh	P	A	A	A	A	A	A	A	A	A	N	N	mineral water	N	common	N	N	N	N	zithromyci	7days	4days	8days	4days	11
sarath	P	A	A	A	A	A	A	P	P	A	N	N	metro water	N	Separate	N	Y	N	N	zithromyci	7days	3days	7days	3days	11.9
devesh	P	A	A	A	A	P	A	P	P	A	Y	N	metro water	N	common	Y	Y	N	N	AXC	14days	12days	15days	3days	11.3
keerthi	A	A	A	A	A	A	A	P	A	A	Y	N	metro water	N	common	N	Y	N	N	zithromyci	7days	4days	7days	3days	11.6
sameera banu	P	A	A	A	A	P	P	P	P	A	N	N	mineral water	N	Separate	N	N	N	Y	zithromyci	7days	2days	5days	2days	11.5
krithi	P	P	A	A	A	P	A	P	P	A	N	N	metro water	N	Separate	N	N	N	N	zithromyci	7days	5days	7days	2days	9.6
ranjith	A	P	A	A	A	A	A	P	P	A	N	N	metro water	N	Separate	N	N	N	N	zithromyci	7days	4days	6days	2days	9.5
preethi	P	P	A	A	A	A	A	P	p	A	N	N	metro water	N	common	Y	N	N	Y	zithromyci	7days	2days	4days	1day	9.1
vignesh	A	P	A	A	A	A	A	P	A	A	N	N	metro water	Y	common	N	N	N	N	zithromyci	7days	3days	7days	4days	10.6
pranesh	P	P	A	A	A	P	A	P	P	A	N	N	mineral water	N	common	N	N	N	N	zithromyci	7days	4days	9days	5days	10.9

Name	TLC	neutrophils	lymphocytes	monocytes	eosinophils	basophils	platelets	Widal H	Widal O	blood culture	sensitivity to ampicillin	cotrimoxazole	chloramphenicol	nalidixic acid	azithromycin	ceftriaxone	repeat blood culture	NARST	MDRST	Ceftriaxone resistant
surya	8600	51.4	38.6	9.2	0.1	0.7	3.3	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
Chandralekha	13900	38	50	11	0.3	0.8	2.36	0	0	S.typhi	R	R	R	R	S	R	sterile	Y	Y	Y
Abhinaya	7400	54	40	3	3	0	2.57	>1:160	>1:160	S.typhi	S	S	S	R	S	R	sterile	Y	N	Y
Sajani	8400	62	31	6	0.7	0.7	1.4	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
Pawan kumar	14200	46.5	46	6.5	0.2	0.8	1.5	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
Adhira krishnan	7600	50	40	8	1	0.9	1.3	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
Narendar	4300	51.7	36.1	11.7	0.1	0.4	2.18	>1:160	>1:160	S.typhi	S	S	S	R	S	R	sterile	Y	N	Y
sabir basha	6100	62	25.1	12.3	0.1	0.5	2.49	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
vijaya kumar	4800	52.6	39.6	7	0.1	0.8	2.44	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
jayashree	12000	54.9	36.4	8.2	0.2	0.3	1.85	>1:160	>1:160	sterile	0	0	0	0	0	0	sterile	0	0	0
vignesh	7500	39.7	44.8	14.9	0	0.6	2.27	>1:160	>1:160	S.typhi	S	S	S	S	S	erately sen	sterile	N	N	N
sabari	5900	36	51.8	9.8	1.5	0.9	2.86	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
praveen kumar	6200	42	44.2	10.7	3	0.1	2.36	>1:160	>1:80	S.typhi	S	S	S	S	S	S	sterile	N	N	N
Rohith	6500	36.4	49.1	10.9	2.8	0.8	3.15	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
Kabilan	5900	50.4	41.2	7.9	0.1	0.4	2.09	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
manimegalai	6600	49	41.5	9.2	0.3	0.1	2.02	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
subburam	4400	60.2	29.4	9.4	0.2	0.8	2.22	>1:160	>1:160	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
sanjay	8400	58	32.6	9.4	0	0	2.6	>1:160	>1:80	S.typhi	S	S	S	R	S	R	sterile	Y	N	Y
sofia rani	14200	50.6	38.2	38.2	0.1	0.4	4.69	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
Nithyashree	6400	54.7	32.2	10.5	1.7	0.9	3.43	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
Karthik	8700	55.1	34.1	10.4	0.1	0.3	3.17	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
Manoranjitham	6900	36	54.8	8.4	0.1	0.7	3	<1:40	<1:30	S.typhi	S	S	S	S	S	S	sterile	N	N	N
prashanth	13300	52.5	40.2	6.7	0.1	0.5	2.31	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
Karthiga	9200	44.3	43.1	12	0.2	0.4	2.12	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
Balavignesh	8400	51.5	39.9	6.9	1.2	0.5	2.81	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
Amith kumar	7700	51	44.3	4.7	0	0	2.57	>1:160	>1:160	S.typhi	S	S	S	R	S	R	sterile	Y	N	Y
rakesh	10200	51.4	40.8	6.6	0.1	1.1	2.28	>1:160	>1:160	S.typhi	S	S	S	R	S	R	sterile	Y	N	Y
yuvashree	7300	52.1	34	11.2	1.7	1	2.1	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
john	9300	44.5	46.4	9.1	0	0	3.07	>1:160	>1:160	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
renuka	8500	60	30	9.4	0.1	0.2	2.65	0	0	S.typhi	S	S	S	R	S	R	sterile	Y	N	Y
dhanesh	7300	44.6	42.4	8.8	3.3	0.6	4.9	<1:20	<1:20	S.typhi	R	R	R	R	S	S	sterile	Y	Y	N
yuvraj	9400	31	53.1	10.3	4.8	0.8	3.9	0	0	S.typhi	S	S	S	R	S	R	sterile	Y	N	Y
mahendran	5200	60	30	9	0.1	0.1	1.45	<1:20	<1:20	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
hemavathi	5900	50	35	14	2.5	0.1	2.5	<1:20	<1:20	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
priscilla	6300	56.9	35.9	6.2	0.1	0.9	2	0	0	S.typhi	S	S	S	R	S	R	sterile	Y	N	Y
sadik	4200	65.4	27	7.6	0	0	2.25	>1:160	>1:160	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
dhanyashri	25100	60.2	23.9	15.1	0.1	0.7	4.33	>1:160	>1:160	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
Gayathri devi	4200	35.9	50.9	12.4	0.1	0.7	1.64	>1:40	<1:20	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
ramakrishnan	7900	44.9	45.8	9.3	0	0	2.17	>1:160	>1:160	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
visakan	5600	55.3	30.2	13.9	0	0.6	2.68	<1:20	<1:20	.paratyphi	S	S	S	S	erate sens	S	sterile	N	N	N
Roseline	8400	53.5	32.9	11	2.4	0.2	3.56	0	0	S.typhi	S	S	S	S	S	erately sen	sterile	N	N	N
Dashwanth	5200	54.1	40.1	5.8	0	0	1.9	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
harikrishnan	5700	61.8	32.4	5.8	0	0	1.36	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
deepika	8000	57.4	33.6	8.1	0.1	0.8	2.24	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
devanandhan	5300	74.9	21.1	4	0	0	1.86	0	0	.paratyphi	S	S	S	R	S	S	sterile	Y	N	N
dharanitharan	7000	68.4	27.3	4.3	0	0	3.44	>1:160	>1:160	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
Abhinaya	6600	51.1	37.3	10.8	0.3	0.5	2.37	0	0	S.typhi	S	R	S	S	S	S	sterile	N	N	N
emancy	12200	40.6	48.2	10.1	0.6	0.5	6.19	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
gomathi	4200	52	46.5	2	0.1	0.1	1.5	0	0	S.typhi	R	R	R	S	S	S	sterile	N	Y	N
hemavathi	7400	68.7	23.4	7.1	0.1	0.7	2.03	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
mahesh	6100	58.3	36.7	5	0	0	1.5	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
ramesh	9300	29	58.8	12.2	0.1	0.1	1.33	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
dharun	6000	60	35.2	4.3	0.1	0.4	1.2	>1:160	>1:160	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
dhanesh	5400	75.7	15.7	8.3	0.1	0.2	2.14	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
sarath	6700	72.6	19.7	7.1	0.1	0.5	2.63	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
devesh	5000	80.9	15.5	2.8	0.5	0.3	65000	>1:160	>1:160	S.typhi	S	S	S	S	S	S	S.typhi	N	N	N
keerthi	4800	52.1	43	4.8	0	0.1	1.96	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
sameera banu	11300	63.4	28.9	7.2	0.1	0.4	2.47	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
krithi	6300	49.6	36.7	11.9	0.5	1.3	1.93	>1:160	>1:40	sterile	0	0	0	0	0	0	0	0	0	0
ranjith	`12000	51.5	39.4	8	0.1	1	2.46	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
preethi	7100	25.9	61.6	11.6	0.2	0.7	2.36	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
vignesh	9400	46.8	36.5	16	0.3	0.4	1.96	<1:20	<1:20	S.typhi	S	S	S	S	S	S	sterile	N	N	N
pranesh	5700	83.9	13	3.1	0	0	1.5	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N

santhosh	5	M	15	intermittent	P	A	A	A	A	A	A	A	A	A	A	A	A	A	Y	P	P	P	P	A	A	A	A	A	P	P	A	N	N	metro water	N	common	N	Y	N	N	ceftriaxone	7days	3days	8days	2days	9.6	8200	46.9	40.8	11.5	0	0.8	2.45	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
dinesh kumar	10	M	14	remittent	P	A	A	A	A	P	A	P	A	A	P	A	P	A	N	A	P	P	A	A	A	P	A	A	P	A	A	Y	N	metro water	N	Separate	Y	Y	N	Y	ceftriaxone	7days	3days	8days	2days	11	8700	64	31.9	4.1	0	0	2.75	0	0	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
kannimozhi	11	F	7	intermittent	P	P	A	A	A	A	A	A	P	A	P	A	A	A	N	A	P	A	P	A	A	A	A	A	P	P	A	N	N	metro water	N	common	N	Y	Y	N	ceftriaxone	7days	3days	11days	5days	11.2	7600	60.7	30.7	8.1	0	0.5	2.43	>1:160	<1:20	S.typhi	S	S	S	S	S	S	sterile	N	N	N
kamalesh	6	M	10	intermittent	A	A	P	A	A	A	A	P	P	A	A	A	A	A	N	A	P	A	P	A	A	A	A	A	A	A	A	N	N	metro water	N	common	N	N	N	N	ceftriaxone	7days	6days	11days	4days	12	6600	56.4	34.5	7.7	0.1	1.3	3.24	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
swarna kumar	11	M	7	intermittent	P	A	A	A	A	A	A	A	A	A	A	A	P	A	N	P	P	P	A	A	A	A	A	A	P	A	A	N	Y	mineral water	N	Separate	Y	N	N	N	ceftriaxone	7days	5days	11days	3days	12.2	9100	51	37.2	11.2	0.1	0.3	2.28	<1:20	<1:20	paratyphi	S	S	S	S	S	S	sterile	N	N	N
madhumeena	2	F	7	intermittent	A	A	A	A	A	A	A	P	P	A	A	P	A	A	N	P	P	P	P	A	A	A	P	A	P	A	A	Y	N	metro water	N	Separate	N	N	N	N	ceftriaxone	10days	7days	13days	3days	8.1	11600	37.1	50.6	12.3	0	0	1.1	0	0	S.typhi	R	R	R	S	S	R	sterile	N	Y	Y
shyam	6	M	8	intermittent	A	A	A	A	A	P	A	P	P	A	P	A	A	A	Y	P	P	P	A	A	A	P	A	P	P	P	A	N	Y	metro water	N	common	N	Y	N	N	ceftriaxone	7days	5days	9days	2days	11.3	8200	45.9	42.8	9.2	1.5	0.6	3.44	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
Boni	9	M	7	intermittent	P	P	A	A	A	A	A	A	P	A	A	A	A	A	N	A	P	P	A	A	A	A	A	P	P	A	A	N	Y	mineral water	N	Separate	N	Y	N	N	ceftriaxone	10days	6days	11days	3days	11.6	6500	64.7	30.3	5	0	0	2.06	>1:160	>1:160	S.typhi	S	S	S	S	S	S	S.typhi	N	N	N
hemalatha	9	F	4	intermittent	A	A	A	A	A	A	A	P	P	A	P	A	A	A	N	P	P	A	A	A	A	A	A	P	P	P	A	Y	N	mineral water	N	Separate	Y	Y	N	N	ceftriaxone	7days	5days	10days	3days	11	4200	52	46.5	2	0.1	0.1	1.5	0	0	S.typhi	R	R	R	S	S	S	sterile	N	Y	N
gomathi	8	F	8	intermittent	A	A	A	A	A	P	A	P	A	A	A	A	A	A	Y	P	P	P	A	A	A	P	A	A	P	P	A	N	N	metro water	Y	Separate	N	N	Y	N	ceftriaxone	7days	6days	15days	5days	10.9	7400	68.7	23.4	7.1	0.1	0.7	2.03	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
Madhesh	2	M	4	intermittent	A	A	A	A	A	P	A	P	P	A	A	A	A	A	N	P	P	P	P	A	A	A	A	A	P	A	A	N	N	metro water	Y	Separate	N	N	N	N	ceftriaxone	7days	3days	7days	2days	9.5	6100	58.3	36.7	5	0	0	1.5	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
monish	2	M	3	intermittent	A	A	A	A	A	A	A	A	A	A	A	A	A	A	Y	A	P	A	P	A	A	A	A	A	P	P	A	N	N	mineral water	N	common	N	N	Y	N	ceftriaxone	7days	3days	8days	4days	10.5	9300	29	58.8	12.2	0.1	0.1	1.33	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
dhanush	8	M	8	intermittent	P	A	A	A	A	A	A	A	P	A	A	A	A	A	N	P	P	P	A	A	A	A	A	A	P	A	A	N	N	metro water	N	Separate	N	Y	N	N	ceftriaxone	7days	3days	8days	4days	12.9	6000	60	35.2	4.3	0.1	0.4	1.2	>1:160	>1:160	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
david	10	M	3	intermittent	A	P	A	A	A	A	A	P	P	A	P	A	A	A	N	P	P	P	A	A	A	A	A	A	A	A	A	N	N	mineral water	N	common	N	N	N	N	ceftriaxone	7days	4days	8days	4days	11	5400	75.7	15.7	8.3	0.1	0.2	2.14	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
saran kumar	10	M	7	intermittent	A	P	P	A	A	A	A	P	A	A	A	A	A	A	N	P	P	P	A	A	A	A	A	A	P	P	A	N	N	metro water	N	Separate	N	Y	N	N	ceftriaxone	7days	3days	8days	3days	11.9	6700	72.6	19.7	7.1	0.1	0.5	2.63	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
devanandhana	9	F	7	intermittent	A	A	A	A	A	P	A	P	P	A	P	A	A	A	N	P	P	P	A	A	A	A	P	A	P	P	A	Y	N	metro water	N	common	Y	Y	N	N	ceftriaxone	14days	12days	15days	3days	11.3	5000	80.9	15.5	2.8	0.5	0.3	65000	>1:160	>1:160	S.typhi	S	S	S	S	S	S	S.typhi	N	N	N
krithika	12	F	7	intermittent	A	A	A	A	A	P	A	P	P	A	P	A	P	A	N	P	P	A	A	A	A	A	A	A	P	A	A	Y	N	metro water	N	common	N	Y	N	N	ceftriaxone	7days	4days	10days	3days	11.6	4800	52.1	43	4.8	0	0.1	1.96	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
smruthi	2	F	5	intermittent	A	A	A	A	A	A	A	P	A	A	P	P	A	A	N	P	P	P	A	A	A	A	P	P	P	P	A	N	N	mineral water	N	Separate	N	N	N	Y	ceftriaxone	7days	2days	9days	2days	11.5	11300	63.4	28.9	7.2	0.1	0.4	2.47	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
sneha	6	F	8	intermittent	A	A	A	A	A	P	A	P	P	A	A	A	A	A	Y	P	P	P	P	A	A	A	P	A	P	P	A	N	N	metro water	N	Separate	N	N	N	N	ceftriaxone	7days	5days	8days	2days	9.6	6300	49.6	36.7	11.9	0.5	1.3	1.93	>1:160	>1:40	sterile	0	0	0	0	0	0	0	0	0	0
yogesh	2	M	7	intermittent	A	A	A	A	A	P	A	A	P	A	A	A	A	A	N	A	P	A	P	A	A	A	A	A	P	P	A	N	N	metro water	N	Separate	N	N	N	N	ceftriaxone	7days	4days	8days	2days	9.5	`12000	51.5	39.4	8	0.1	1	2.46	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
pritika	2	F	11	intermittent	A	A	A	A	A	A	A	P	A	A	A	A	A	A	N	P	P	P	P	A	A	A	A	A	P	p	A	N	N	metro water	N	common	Y	N	N	Y	ceftriaxone	7days	2days	7days	1day	9.1	7100	25.9	61.6	11.6	0.2	0.7	2.36	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
ganesh	2	M	5	intermittent	A	A	A	A	A	P	A	A	A	A	A	A	A	A	N	A	P	A	P	A	A	A	A	A	P	A	A	N	N	metro water	Y	common	N	N	N	N	ceftriaxone	7days	3days	8days	4days	10.6	9400	46.8	36.5	16	0.3	0.4	1.96	<1:20	<1:20	S.typhi	S	S	S	S	S	S	sterile	N	N	N
parthiban	12	M	7	intermittent	A	A	A	A	A	A	A	P	P	A	P	A	A	A	N	P	P	P	P	A	A	A	A	P	P	P	A	N	N	mineral water	N	common	N	N	N	N	ceftriaxone	7days	4days	11days	5days	10.9	5700	83.9	13	3.1	0	0	1.5	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
sethupriya	8	F	9	intermittent	A	P	P	A	A	P	A	P	A	A	P	A	P	A	N	P	P	P	P	A	A	A	A	A	P	P	A	N	N	metro water	Y	Separate	N	N	N	N	ceftriaxone	7days	3days	8days	1day	10.1	4100	38.1	54	7.9	0	0	1.55	>1:160	>1:40	S.typhi	S	S	S	S	S	S	sterile	N	N	N
rakesh	6	M	3	intermittent	P	A	A	A	A	P	A	P	A	A	A	A	A	A	N	P	P	A	P	A	A	A	A	A	P	P	A	N	Y	metro water	N	common	N	Y	N	N	ceftriaxone	7days	4days	10days	4days	10.5	5000	82	15	2.8	0	0.2	3	<1:!60	<1:20	S.typhi	S	S	S	R	S	S	sterile	Y	N	N
megala	4	F	7	intermittent	P	A	A	A	A	P	A	A	P	A	A	P	A	A	Y	P	P	P	P	A	A	A	P	P	P	P	A	N	N	metro water	N	common	N	Y	N	N	ceftriaxone	7days	2days	7days	1day	10	5800	42.2	52.3	5.5	0	0	1.5	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
archana	10	F	5	intermittent	P	A	P	A	A	P	A	P	P	A	A	A	A	A	N	P	P	P	P	A	P	A	A	A	A	A	A	N	N	metro water	N	common	N	N	N	N	ceftriaxone	7days	3days	10days	3days	12.5	11100	74.7	18.5	5.9	0.1	0.8	2.9	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
malar	4	F	25	intermittent	P	A	A	A	A	P	A	P	P	A	A	A	A	A	Y	P	P	P	P	A	A	A	P	A	P	P	A	N	N	mineral water	N	common	N	N	N	N	ceftriaxone	7days	4days	9days	2days	8.4	18700	24	63.9	12.1	0	1	1.5	<1:20	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
mounica	10	F	7	intermittent	A	A	P	A	A	P	A	A	A	A	A	A	P	A	Y	A	P	A	A	A	A	A	A	A	P	P	A	Y	N	metro water	N	Separate	N	Y	N	N	ceftriaxone	7days	3days	7days	3days	12.5	6100	59.7	35.4	4.9	1.89	0	0	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
karthikeyan	10	M	5	intermittent	P	P	A	A	A	P	A	P	P	A	A	A	A	A	Y	P	P	P	A	A	A	A	A	A	P	P	A	Y	N	metro water	N	Separate	N	N	N	N	ceftriaxone	7days	5days	11days	5days	11.7	10100	86.3	11.2	1.6	0	0.9	1.58	>1:40	>1:20	S.typhi	S	S	S	S	S	S	sterile	N	N	N
balamurugan	3	M	10	intermittent	P	A	A	A	A	A	A	P	P	A	P	A	P	A	N	P	P	P	P	A	A	A	A	A	P	A	A	Y	N	metro water	Y	Separate	N	Y	N	N	ceftriaxone	7days	2days	9days	3days	9.1	6900	44.7	50.3	5	0.2	0.2	2.29	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
silverstom	8	M	14	intermittent	P	A	A	A	A	A	A	A	P	A	A	A	A	A	Y	A	P	P	A	A	A	A	A	P	P	A	A	N	Y	mineral water	N	Separate	N	Y	N	N	ceftriaxone	7days	6days	10days	1day	12.6	7700	51.3	32.8	15.1	0.2	0.6	2.71	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
karish	2	M	15	intermittent	A	A	A	A	A	A	A	A	A	A	A	A	P	A	N	A	P	A	P	A	A	A	A	A	P	P	A	N	Y	mineral water	N	Separate	N	N	N	N	ceftriaxone	7days	2days	10days	3days	7.6	8700	34.5	43.9	18	3	0.6	2.51	>1:40	>1:20	S.typhi	S	S	S	S	S	S	sterile	N	N	N
janani	7	F	9	intermittent	P	A	A	A	A	A	A	A	A	A	A	A	P	A	N	P	P	P	P	A	A	A	A	P	P	A	A	N	N	metro water	N	Separate	N	N	N	N	ceftriaxone	7days	4days	7days	1day	10.5	6100	54.7	38.6	6.7	0	0	2.73	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
kamalesh	6	M	10	intermittent	A	A	P	A	A	A	A	P	A	P	A	A	A	A	N	A	P	A	P	A	A	P	A	P	P	A	A	N	N	metro water	N	Separate	N	N	N	N	ceftriaxone	7days	5days	8days	2days	12	6600	56.4	34.5	7.7	0.1	1.3	3.24	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
shivani	3	F	10	intermittent	P	A	A	A	A	A	A	A	A	A	A	A	P	A	N	P	P	P	P	A	A	A	A	A	P	A	A	Y	N	metro water	N	common	Y	N	N	Y	ceftriaxone	7days	6days	10days	3days	10.6	17700	53.1	38.1	8.1	0	0.7	3.85	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
shwetha	6	F	7	intermittent	P	P	A	A	A	P	A	A	A	A	A	A	P	A	Y	A	P	P	P	A	A	A	A	A	P	P	A	N	N	mineral water	N	common	N	Y	N	N	ceftriaxone	7days	2days	7days	1day	10	4700	53.7	39.9	6.4	0.5	0.3	1.67	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
pavithra	11	F	14	intermittent	P	A	A	A	A	P	A	P	A	A	P	A	A	A	N	A	P	P	P	A	A	A	A	A	P	P	A	N	N	mineral water	N	Separate	N	Y	N	N	ceftriaxone	7days	2days	7days	1day	12.4	5700	58.7	29	11.9	0	0.4	1.61	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
muskan banu	6	F	5	intermittent	A	P	A	A	A	A	A	P	A	A	P	A	A	A	Y	A	P	A	P	A	A	A	A	A	P	A	A	N	N	mineral water	N	Separate	N	N	N	N	ceftriaxone	7days	2days	10days	4days	10.9	8300	59	34.2	6.6	0.1	0.1	1.67	<1:20	<1:20	S.typhi	erately sen	S	S	S	erately sen	S	sterile	N	N	N
naveen kumar	11	M	4	intermittent	A	P	A	A	A	A	A	P	P	A	P	A	A	A	N	A	P	P	A	A	A	A	A	P	P	P	A	N	Y	metro water	N	common	N	N	N	N	ceftriaxone	7days	5days	10days	3days	10	6800	50.5	42	8.5	1	1	1.5	>1:160	>1:80	S.typhi	S	S	S	S	S	S	sterile	N	N	N
swetha	11	F	4	intermittent	A	A	A	A	A	A	A	A	P	A	P	A	A	A	Y	P	P	A	A	A	A	A	A	P	P	A	A	N	N	metro water	N	common	N	Y	N	N	ceftriaxone	7days	3days	10days	3days	11.7	6700	62.7	24.6	12.2	0.1	0.4	1.9	>1:20	>1:20	S.typhi	S	S	S	S	S	S	sterile	N	N	N
rajesh kumar	9	M	11	intermittent	A	P	A	A	A	A	A	A	A	A	A	A	A	A	Y	A	P	P	P	A	A	A	A	A	P	P	A	Y	N	mineral water	N	Separate	N	Y	N	N	ceftriaxone	7days	4days	11days	4days	12.6	9900	53.4	28.8	10.7	6.7	0.4	3.77	>1:20	>1:40	s.paratyhi A	S	S	S	S	S	S	sterile	N	N	N
dinesh	3	M	5	intermittent	A	A	P	A	A	P	A	P	A	A	A	A	A	A	N	A	P	P	P	A	A	A	A	A	P	A	A	N	N	metro water	Y	Separate	N	Y	N	N	ceftriaxone	7days	3days	8days	3days	10.1	10900	66	27	7	0	0	1.91	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
harini	9	F	4	intermittent	A	A	A	A	A	A	A	P	A	A	P	A	A	A	Y	A	P	A	A	A	A	A	A	A	A	A	A	N	N	mineral water	N	common	N	Y	N	Y	ceftriaxone	7days	3days	11days	5days	10.3	7500	60.8	29.6	9.6	0	0	2.99	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
sanjay manohar	7	M	7	intermittent	A	A	A	A	A	A	A	P	A	A	A	A	P	A	Y	P	P	A	A	A	A	A	A	A	P	P	A	N	N	metro water	Y	Separate	N	N	N	N	ceftriaxone	7days	3days	8days	3days	11.3	3800	47.2	42.4	8.9	0.9	0.6	2.42	<1:20	<1:20	S.typhi	S	S	S	S	S	S	sterile	N	N	N
mencila	11	F	10	intermittent	P	A	A	A	A	P	A	A	A	A	A	A	A	A	N	A	P	A	A	A	A	A	A	A	A	A	A	Y	N	metro water	N	common	N	Y	N	N	ceftriaxone	7days	4days	10days	3days	11.8	8500	50	42	7.2	0.1	0.7	0.79	>1:160	>1:160	sterile	0	0	0	0	0	0	0	0	0	0
iniya	6	F	5	intermittent	A	A	A	A	A	A	A	P	P	A	P	A	A	A	N	A	p	A	A	A	A	A	A	P	P	P	A	N	N	metro water	N	common	Y	N	N	Y	ceftriaxone	7days	3days	8days	3days	11.1	5900	48.5	39.3	11.5	0.1	0.6	1.2	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
abubakkar siddiqi	4	M	10	intermittent	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	P	P	P	P	A	A	A	A	A	P	P	A	Y	N	metro water	N	common	N	Y	Y	N	ceftriaxone	7days	4days	10days	3days	10	8800	40.3	52.2	7.5	0	0	2.73	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
harish	11	M	10	intermittent	A	A	A	A	A	P	A	P	A	A	A	A	A	A	Y	A	P	P	A	A	A	A	A	P	P	A	A	N	N	Metro water	N	Separate	N	Y	N	N	ceftriaxone	7days	3days	9days	2days	11.3	8600	51.4	38.6	9.2	0.1	0.7	3.3	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
meena	2	F	5	intermittent	P	A	A	A	A	P	A	A	P	A	A	A	A	A	N	P	P	P	P	A	A	A	A	A	P	P	A	N	N	Metro water	N	Separate	N	N	N	N	ceftriaxone	7days	5days	11days	5days	10	13900	38	50	11	0.3	0.8	2.36	0	0	S.typhi	R	R	R	R	S	R	sterile	Y	Y	Y
jayashree	10	F	9	intermittent	A	A	A	A	A	A	A	P	P	A	P	A	A	A	N	P	P	P	A	A	A	A	A	A	P	P	A	N	Y	Metro water	N	Separate	N	N	N	N	ceftriaxone	7days	4days	9days	2days	11.6	7400	54	40	3	3	0	2.57	>1:160	>1:160	S.typhi	S	S	S	R	S	R	sterile	Y	N	Y
devika	2	F	7	intermittent	A	A	A	A	A	A	P	P	A	P	A	A	A	A	N	P	P	P	P	A	A	A	P	A	P	P	A	N	N	Metro water	N	Separate	N	N	N	N	ceftriaxone	7days	5days	9days	2days	9.5	8400	62	31	6	0.7	0.7	1.4	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
rithesh	2	M	6	intermittent	A	A	A	A	A	P	A	A	A	A	A	A	A	A	N	P	P	P	P	A	A	A	A	A	P	A	A	N	N	Metro water	N	Separate	N	N	N	N	ceftriaxone	7days	4days	9days	2days	10	14200	46.5	46	6.5	0.2	0.8	1.5	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
avinashi	8	F	7	intermittent	P	A	A	A	A	A	A	A	A	A	P	A	A	A	N	P	P	P	A	A	A	A	A	A	P	A	A	N	N	Metro water	N	Separate	N	N	N	N	ceftriaxone	7days	3days	8days	1day	11	7600	50	40	8	1	0.9	1.3	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
yogesh	5	M	5	intermittent	A	A	A	A	A	A	A	A	A	A	A	A	A	A	N	A	P	P	P	A	A	P	A	A	P	P	A	N	N	Mineral water	N	Separate	Y	N	N	N	ceftriaxone	7days	6days	10days	2days	10.6	4300	51.7	36.1	11.7	0.1	0.4	2.18	>1:160	>1:160	S.typhi	S	S	S	R	S	R	sterile	Y	N	Y
makbul khan	10	M	9	intermittent	P	A	A	A	A	P	A	P	A	A	P	A	A	A	N	P	P	P	A	A	A	A	A	A	P	P	A	Y	N	Metro water	N	common	N	Y	Y	Y	ceftriaxone	7days	5days	7days	1day	12	6100	62	25.1	12.3	0.1	0.5	2.49	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
vijay	6	M	15	intermittent	P	A	A	A	A	P	A	A	A	A	P	A	P	A	Y	A	P	A	P	A	A	P	A	A	P	A	A	N	N	Metro water	N	common	N	N	Y	N	ceftriaxone	7days	3days	10days	4days	10.2	4800	52.6	39.6	7	0.1	0.8	2.44	>1:160	>1:160	S.typhi	S	S	S	S	S	S	sterile	N	N	N
aruna	7	F	7	intermittent	P	A	A	A	A	A	A	P	A	A	P	A	P	A	N	A	P	A	A	A	A	P	A	P	P	P	A	N	N	Mineral water	N	common	N	N	N	N	ceftriaxone	7days	5days	9days	3days	11.6	12000	54.9	36.4	8.2	0.2	0.3	1.85	>1:160	>1:160	sterile	0	0	0	0	0	0	sterile	0	0	0
vinayak	4	M	4	intermittent	P	A	A	A	A	A	A	P	P	A	A	P	A	A	N	P	P	P	P	A	A	P	A	A	P	A	A	N	N	Metro water	Y	Separate	N	Y	N	N	ceftriaxone	14days	12days	17days	6days	8.1	7500	39.7	44.8	14.9	0	0.6	2.27	>1:160	>1:160	S.typhi	S	S	S	S	S	erately sen	sterile	N	N	N
saravanan	4	M	4	intermittent	P	A	A	A	A	P	P	A	A	A	A	A	A	A	N	A	P	A	P	A	A	A	A	P	P	P	A	Y	N	Metro water	N	Separate	N	N	N	N	ceftriaxone	7days	3days	10days	4days	10.9	5900	36	51.8	9.8	1.5	0.9	2.86	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
jayesh	7	M	10	intermittent	P	P	A	A	A	P	A	A	A	A	A	A	A	A	N	A	P	P	P	A	A	A	A	A	P	P	A	N	N	Metro water	Y	common	N	N	N	N	ceftriaxone	7days	3days	9days	2days	11	6200	42	44.2	10.7	3	0.1	2.36	>1:160	>1:80	S.typhi	S	S	S	S	S	S	sterile	N	N	N
rahul	6	M	7	intermittent	P	P	A	A	A	A	A	A	A	A	A	A	P	A	Y	A	P	A	A	A	A	A	A	A	P	A	A	Y	N	Metro water	N	Separate	N	Y	Y	N	ceftriaxone	7days	4days	9days	2days	11.1	6500	36.4	49.1	10.9	2.8	0.8	3.15	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N
sarathy	10	M	10	intermittent	P	P	P	A	A	A	P	A	P	A	P	A	A	A	Y	P	P	P	A	A	A	A	A	A	P	P	A	N	N	Mineral water	N	Separate	N	N	N	N	ceftriaxone	7days	4days	11days	5days	11.9	5900	50.4	41.2	7.9	0.1	0.4	2.09	0	0	S.typhi	S	S	S	S	S	S	sterile	N	N	N

crossover to ceftriaxone/ prolonged treatment with ceftriaxone
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ANNEXURE - I

STUDY PROFORMA

Name:

Age: Sex: DOB :

Address/Phone number:

School:

Insurance number:

Date of admission: Date of discharge:

Diagnosis:

History:

- Fever :
    a. Duration -
    b. Pattern -
    c. Chills/Rigors -
    d. Response to antipyretics -
- Headache :
- Myalgia :
- Altered sensorium :
- Seizures :
- Anorexia :
- Loss of weight :
- Vomiting :
- Diarrhoea :
- Constipation :
- Abdominal pain :
- Distension of abdomen :

- Cough :
- Breathlessness :

Treatment history:

Examination:

- Toxic :
- Febrile/ afebrile :
- Hydration :
- Coated tongue :
- Glossitis :
- cheilitis :
- pallor :
- icterus :
- Vitals PR
  RR
  BP
- Skin (rose spots) :
- Lymphadenopathy :
- CVS :
- RS :
- Abdomen :
  a. Distension -
  b. Tenderness -
  c. Hepatomegaly -
  d. Splenomegaly -
  e. Fluid/tympanitic note -
  f. Bowel sounds -
- CNS :

Others:

Complications if any:

Anthropometry: Weight - Height -
MAC -

Family & Socioeconomic history:

- Any other member/sibling affected :
- Anyone in the neighbourhood :
- Water supply (Potable/not) :
- Boiled /not :
- Sanitary latrine :
- Immunisation (Typhoid) :
- Diet (Salads/eating out) :
- Past history of typhoid in mother :
- Past history of typhoid in the child :
- Food handling habits in the mother :

Treatment given:

- Medication, route & dose :
- Duration of therapy :
- Time taken for response :
- Duration of hospital stay :
- Mean duration at diagnosis :
- Diagnosed on what day of fever :

Investigations:

Hb				
TLC				
DLC N				
L				
M				
E				
B				
platelets				
LFT TSB				
D				
I				
SGOT				
SGPT				
ALP				
Widal H				
O				
Blood culture				
Urine culture				
Stool culture				
Drug sensitivity				
Resistance				
Stool culture after 1 month				

ANNEXURE - II

KEYWORDS

MDRST: Multi drug resistant Salmonella typhi

NARST: Nalidixic acid resistant Salmonella typhi

CBC: Complete blood count

Hb: Hemoglobin

TLC: Total leucocyte count

SD: Standard deviation

SE: Standard error

MIC: Minimum inhibitory concentration

C/S: Culture sensitivity

IV: Intra venous

OD: Once daily

BD: Twice daily

ANNEXUIRE - III

CONSENT FORM

I, ……., have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent for my child to be included as a participant in the study called **"Effectiveness of Azithromycin in treating uncomplicated Enteric fever as compared to parenteral Ceftriaxone" : An Experimental study, ESI-PGIMSR, KK Nagar, Chennai, 2012-2013.**

(1) I have read and understood this consent form and the information provided to me.

(2) I have had the consent document explained to me.

(3) I have been explained about the nature of the study.

(4) My rights and responsibilities have been explained to me by the investigator.

(5) I agree to cooperate with the investigator

(6) Currently I'm not participating in any research study.

(7) I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future.

(8) I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the

regulatory authorities, Government agencies, and ethics committee. I understand that they may inspect my original records.

(9) My child's identity will be kept confidential if my data are publicised.

(10) I have had my questions answered to my satisfaction.

(11) I have decided to be in the research study.

I am aware, that if I have any questions during this interview, I should contact at one of the addresses listed above. By signing this consent from, I attest that the information given in this document has been clearly explained to me and understood by me.

As I was not able to read, the consent form has been read out to me by the investigator and all my questions have been answered. I give my consent with my free will.

Name of Participant_____ Signature of Participant _____

Date:

Name of witness_____ Signature of witness _____

Date: **Thumb print of participant**

SIGNATURE OF THE INVESTIGATOR:

DATE: